

Peri-implant health and disease. A systematic review of current epidemiology

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Abstract

Background: To develop preventive strategies addressing peri-implant diseases, a thorough understanding of the epidemiology is required.

Aim: The aim was to systematically assess the scientific literature in order to evaluate the prevalence, extent and severity of peri-implant diseases.

Material & Methods: Data were extracted from identified studies. Meta-analyses for prevalence of peri-implant mucositis and peri-implantitis were performed. The effect of function time and disease definition on the prevalence of peri-implantitis was evaluated by meta-regression analyses. Data on extent and severity of peri-implant diseases were estimated if not directly reported.

Results: Fifteen articles describing 11 studies were included. Case definitions for mucositis and peri-implantitis varied. The prevalence of peri-implant mucositis and peri-implantitis ranged from 19 to 65% and from 1 to 47%, respectively. Meta-analyses estimated weighted mean prevalences of peri-implant mucositis and peri-implantitis of 43% (CI: 32–54%) and 22% (CI: 14–30%), respectively. The meta-regression showed a positive relationship between prevalence of peri-implantitis and function time and a negative relationship between prevalence of peri-implantitis and threshold for bone loss. Extent and severity of peri-implant diseases were rarely reported.

Conclusion: Future studies on the epidemiology of peri-implant diseases should consider (i) applying consistent case definitions and (ii) assessing random patient samples of adequate size and function time.

Key words: Incidence; Peri-implant disease; Prevalence

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Peri-implant mucositis is defined as the presence of a plaque-related inflammatory soft tissue infiltrate without concurrent loss of peri-implant bone tissue, while peri-implantitis should demonstrate inflammation in combination with bone loss (Albrektsson & Isidor 1994, Zitzmann & Berglundh 2008).

At the 7th EWOP, similarities and differences between periodontal and peri-implant diseases were addressed, focusing on host response and bacterial challenge characteristics (Lang & Berglundh 2011). The importance of prevention was highlighted, as mucositis was found to be potentially progressing into peri-implantitis if left untreated, but reversible if adequately treated.

At the 6th European Workshop on Periodontology (EWOP), issues related to peri-implant diseases were discussed. Mucositis was found to occur in more than 50% of all

implant-carrying subjects, while peri-implantitis was found to affect between 28% and 56% of subjects (Lindhe & Meyle 2008). The observed variability for reported prevalence of peri-implant diseases between different studies may be explained, in part, by methodological issues, such as the heterogeneous use of case definitions (Tomasi & Derks 2012).

At the 8th EWOP, the occurrence of biological complications at dental implants was identified as a main outcome domain when evaluating the efficacy of implant therapy (Tonetti & Palmer 2012). To facilitate future

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research and overcome problems highlighted by Tomasi & Derks (2012), case definitions for peri-implant mucositis and peri-implantitis were suggested by Sanz & Chapple (2012).

As the outcome of therapy of peri-implantitis is still considered unpredictable (Lindhe & Meyle 2008), it appears crucial to focus on prevention. In order to develop appropriate preventive strategies addressing peri-implant diseases, a thorough understanding of the epidemiology in terms of prevalence as well as extent and severity of mucositis and peri-implantitis is required. The aim of the present systematic review was to assess the scientific literature in order to evaluate the prevalence, extent and severity of peri-implant diseases.

Material and Methods

Focus question

This review was performed according to the PRISMA guidelines (Liberati et al. 2009, see Appendix 1). The focus question was: "In patients with osseointegrated dental implants, what are the prevalence, extent and severity of peri-implant diseases?" Following the PICO structure, implant-carrying subjects were considered as the population. No definitions for intervention/exposure or comparison were made. Prevalence of peri-implant mucositis and/or peri-implantitis was defined as an outcome.

Inclusion criteria

Studies evaluating the incidence or prevalence of peri-implant mucositis and peri-implantitis were considered for this systematic review.

For the incidence of peri-implant diseases, prospective longitudinal studies were eligible. For the assessment of prevalence, cross-sectional studies were considered. No limits were applied in regard to minimum function time of implants. Only studies reporting on samples of at least 100 subjects were included. To be eligible articles should report subject-level data.

Search strategy

An electronic search of three databases (MEDLINE via Pubmed,

EMBASE via Ovid and Cochrane database) was performed in March 2014. The search algorithm is described in Table 1.

In addition, a hand search was performed including (i) reference lists, (ii) previous systematic reviews and (iii) the following scientific journals: *Clinical Implant Dentistry and Related Research*, *Clinical Oral Implants Research*, *European Journal of Oral Implants*, *Implant Dentistry*, *International Journal of Oral and Maxillofacial Implants*, *International Journal of Periodontics and Restorative Dentistry*, *Journal of Oral and Maxillofacial Surgery*, *Journal of Clinical Periodontology*, *Journal of Periodontal Research* and *Journal of Periodontology*.

Titles of all identified studies were screened for eligibility. Abstracts were then studied and selected independently by the two reviewers. The level of agreement was calculated (*k*-score). Relevant articles were analysed in full-text and disagreement was resolved by discussion.

Quality of reporting

In order to assess the quality of reporting the STROBE checklist (Vandenbroucke et al. 2007, von Elm et al. 2008) was applied. The items on the checklist (see Appendix 1) were assessed for each of the included articles as (i) present, (ii) not present or (iii) not applicable. The total adherence was expressed as percentage of items present.

Peri-implant diseases

Evidence tables were constructed to extract information on research methodology, case definitions and implant loss from all publications included in the review. Distinctions were made between studies assessing marginal bone loss, i.e. changes of bone levels over time, and reports assessing marginal bone levels, i.e. assessments at a single time point. Prevalence or incidence of peri-implant mucositis and peri-implantitis were recorded as reported in the articles. As information on incidence

Table 1. Algorithm for electronic search

Focus question	In patients with osseointegrated dental implants, what are the prevalence, extent and severity of peri-implant diseases?	
Population	Dental implant: "dental implants"[MeSH Terms] OR ("dental"[All Fields] AND "implants"[All Fields]) OR "dental implants"[All Fields] OR ("dental"[All Fields] AND "implant"[All Fields]) OR "dental implant"[All Fields]	
	Dental implantation: "dental implantation"[MeSH Terms] OR ("dental"[All Fields] AND "implantation"[All Fields]) OR "dental implantation"[All Fields]	OR
	Dental implants: "dental implants"[MeSH Terms] OR ("dental"[All Fields] AND "implants"[All Fields]) OR "dental implants"[All Fields]	
Outcome	Disease: "disease"[MeSH Terms] OR "disease"[All Fields]	AND
	Peri-implantitis: "peri-implantitis"[MeSH Terms] OR "peri-implantitis"[All Fields] OR ("peri"[All Fields] AND "implantitis"[All Fields]) OR "peri implantitis"[All Fields]	
	Mucositis: "mucositis"[MeSH Terms] OR "mucositis"[All Fields]	OR
	Alveolar bone loss: "alveolar bone loss"[MeSH Terms] OR ("alveolar"[All Fields] AND "bone"[All Fields] AND "loss"[All Fields]) OR "alveolar bone loss"[All Fields]	
	Bone resorption: "bone resorption"[MeSH Terms] OR ("bone"[All Fields] AND "resorption"[All Fields]) OR "bone resorption"[All Fields]	
Limits	Humans; English; Not review	

of peri-implant diseases was limited, data were not analysed separately.

Meta-analyses were performed to estimate overall prevalence of peri-implant mucositis and peri-implantitis (OpenMeta[Analyst]) (Wallace et al. 2012). The binary random-effects method was chosen. Results were presented as Forest plots with weighted mean values and 95% confidence intervals (CI). Inconsistency was expressed by I^2 .

The effect of time on the prevalence of peri-implantitis was evaluated by identifying a homogenous group of studies covering different function times. For this purpose, studies using bone level assessments of similar magnitude were selected.

In addition, to evaluate the impact of chosen threshold for bone loss on the prevalence of peri-implantitis, relevant studies were selected. Meta-regression analyses (random effects model) were performed and the p -value of the covariate coefficient was calculated.

Extent and severity of peri-implant diseases

Included studies were scrutinised for data on extent, i.e. the number of affected implants in affected patients, and severity, i.e. the degree of bone loss and/or probing pocket depth at affected implants. If direct information was not reported, an attempt to

estimate the extent of peri-implant disease was performed. Thus, the ratio between the number of affected implants and the total number of implants present in the affected patient group was calculated.

Results

The electronic search identified 3840 articles. Following screening of titles, 274 papers were selected for evaluation of abstracts. The hand search revealed three additional papers resulting in 277 potentially relevant articles. After independent selection of abstracts by the two reviewers, 27 articles were analysed in full-text (Fig. 1). The measure of agreement

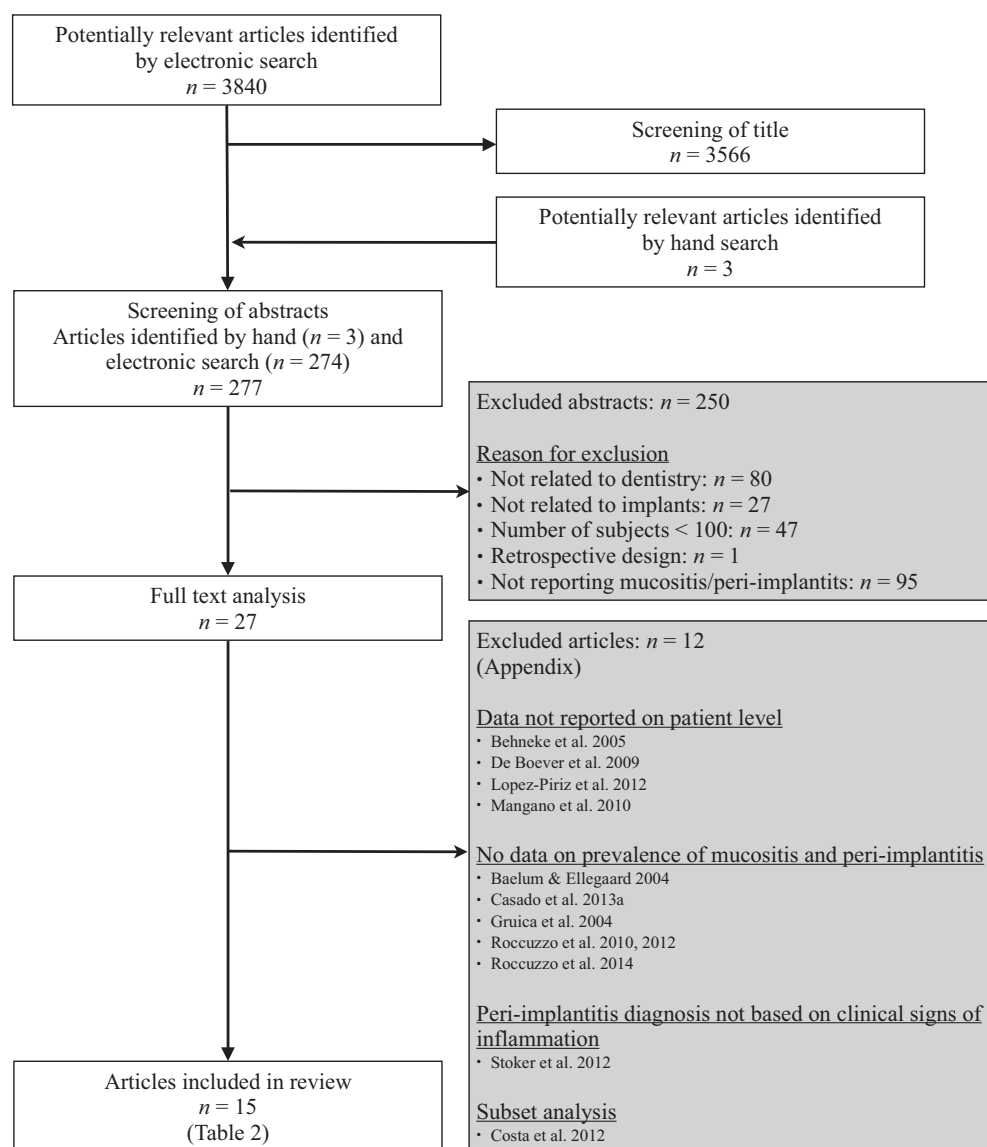


Fig. 1. Flow-chart of study selection.

was $k = 0.92$. Excluded studies and reasons for exclusion are described in the Appendix 1. Finally, 15 articles describing 11 studies were included in the present review (Table 2).

Quality of reporting

Results of the assessment of quality of reporting according to the STROBE checklist are reported in Table 3. The adherence to the STROBE criteria varied between 55% and 77%.

Implant loss

Implant loss was reported in five of the included studies and ranged from 0 to 13.6% at the patient level and from 0 to 8.3% at the implant level.

Case definitions

For details on case definitions see Table 2.

Mucositis

Two studies defined mucositis as the presence of bleeding on probing (BoP) without concomitant bone loss (Ferreira et al. 2006, Casado et al. 2013b).

A total of four studies used measurements of bone level in conjunction with assessments of BoP (Roos-Jansåker et al. 2006, Máximo et al. 2008, Mir-Mari et al. 2012, Marrone et al. 2013). Thresholds for marginal bone levels varied from <1 to <3 threads.

Koldslund et al. (2010) and Cecchinato et al. (2013, 2014) assessed bone loss and defined mucositis as the presence of BoP and bone loss ≤ 0.4 mm and ≤ 0.5 mm, respectively.

Peri-implantitis

Two studies used assessments of inflammation and bone levels to define peri-implantitis without specifying a specific threshold (Ferreira et al. 2006, Dvorak et al. 2011).

A total of three studies (Máximo et al. 2008, Mir-Mari et al. 2012, Marrone et al. 2013) used assessments of inflammation and bone levels, including thresholds when defining peri-implantitis. The thresholds for marginal bone levels varied from ≥ 2 threads to >2 mm.

In six studies, bone loss in addition to inflammation was assessed for

diagnosis of peri-implantitis. Casado et al. (2013b) defined peri-implantitis as the presence of BoP and bone loss, without specifying any radiographic threshold. For the remaining studies (Fransson et al. 2005, 2008, Roos-Jansåker et al. 2006, Koldslund et al. 2010, Zetterqvist et al. 2010, Cecchinato et al. 2013, 2014), thresholds for marginal bone loss varied from >0.4 mm to >5 mm.

The reference time points for assessments of bone loss differed between the studies. One study evaluated bone loss in relation to baseline radiographs taken after implant surgery (Casado et al. 2013b). Two studies used prosthetic loading as the reference time point (Koldslund et al. 2010, Zetterqvist et al. 2010) while three studies used the 1-year examination after loading as reference (Fransson et al. 2005, 2008, Roos-Jansåker et al. 2006, Cecchinato et al. 2013, 2014).

Peri-implant diseases

Eleven studies (15 articles) evaluated the prevalence of peri-implant diseases (Table 2). The number of patients included varied from 100 to 662 subjects. The mean function time ranged from 3.4 to 11.0 years.

Mucositis

The prevalence of peri-implant mucositis was assessed in eight of the studies. The two studies not including any threshold for bone level and bone loss reported a prevalence for peri-implant mucositis of 19% (Casado et al. 2013b) and 65% (Ferreira et al. 2006), respectively.

The studies including assessments of bone levels in the definition of peri-implant mucositis (Roos-Jansåker et al. 2006, Máximo et al. 2008, Mir-Mari et al. 2012, Marrone et al. 2013) reported prevalences ranging from 31 to 48%.

The two studies evaluating bone loss to define mucositis reported a prevalence of mucositis of 39% (Koldslund et al. 2010) and 65% (Cecchinato et al. 2014), respectively.

Peri-implantitis

The prevalence of peri-implantitis was 24% (Dvorak et al. 2011) and 9% (Ferreira et al. 2006) in the two studies not including any thresholds for assessments of bone levels.

The three studies using assessments of bone levels including different thresholds reported a prevalence of peri-implantitis ranging from 12 to 37% (Máximo et al. 2008, Mir-Mari et al. 2012, Marrone et al. 2013).

The one study assessing bone loss without establishing any threshold reported a prevalence of 30% (Casado et al. 2013b).

The remaining four studies assessing bone loss with different thresholds reported a prevalence of peri-implantitis ranging from 1 to 47% (Fransson et al. 2005, 2008, Roos-Jansåker et al. 2006, Koldslund et al. 2010, Zetterqvist et al. 2010).

Meta-analyses of the prevalence of peri-implant diseases

The meta-analyses of prevalences of peri-implant diseases revealed weighted mean values of 42.9% (95% CI 32–54%) and 21.7% (95% CI 14–30%) for mucositis and peri-implantitis, respectively (Figs 2 and 3). Inconsistency, expressed as I^2 , was 94 and 97%, respectively.

Results of the meta-regression (Figs 4a and 4b) showed a statistically significant positive relationship between the prevalence of peri-implantitis and mean function time (Coefficient: 0.044, p -value <0.001). A statistically significant negative relationship was shown between the prevalence of peri-implantitis and threshold for marginal bone loss (Coefficient: -0.069 , p -value <0.001).

Extent and severity of peri-implant diseases

Mucositis

None of the included studies reported on the extent of mucositis. The estimated extent ranged from 33 to 100% (Table 2).

Degrees of severity of peri-implant mucositis could be assessed in one study (Roos-Jansåker et al. 2006). While 48% of all patients were diagnosed with mucositis (Probing pocket depth (PPD) ≥ 4 mm, BoP & bone level <1 thread), the prevalence of subjects presenting mucositis in conjunction with greater PPD was lower (PPD ≥ 5 mm: 16% and PPD ≥ 6 mm: 4%).

Table 2. Included studies ($n = 11$ studies, 15 articles)

First author, year	Study design & function time	Site, setting & funding	Sampling & sample size	Implant loss	Case definition	Prevalence of mucositis	Prevalence of peri-implantitis	Extent and severity of peri-implant diseases
Casado et al. (2013b)	Cross-sectional 1–5 years mean: not reported	Brazil University Instituit-ional	Convenience Initial: 103 Assessed: 103	Not reported	<i>Mucositis:</i> BoP & absence of bone loss <i>Peri-implantitis:</i> BoP & bone loss from implant surgery, no threshold <i>Mucositis:</i> BoP & bone loss ≤ 0.5 mm <i>Peri-implantitis:</i> PPD ≥ 4 mm, BoP & bone loss > 0.5 mm from ≥ 1 year after loading	Patient level: 19.4%	Patient level: 30.1%	<i>Mucositis:</i> Not reported <i>Peri-implantitis:</i> Not reported
Cecchinato et al. (2013, 2014)	Cross-sectional ≥ 8 years mean: ≥ 10.7 years	Italy Private Industry	Convenience Initial: 133 Assessed: 100	Patient level: 7% Implant level: 4%		Patient level: 65% Implant level: 69.8%	Patient level: 23% Implant level: 11.3%	<i>Mucositis:</i> Estimated extent: 100% Severity: not reported <i>Peri-implantitis:</i> Estimated extent: 46.3% Severity (different case definitions): • PPD ≥ 4 mm, BoP & bone loss > 1.0 mm: 16% • PPD ≥ 4 mm, BoP & bone loss > 2 mm: 7%
Dvorak et al. (2011)	Cross-sectional 1–24 years mean: 6.0 years	Austria University Instituit-ional	Convenience (post-menopausal women) Initial: 203 Assessed: 177	Patient level: 13.6% Implant level: 8.3%	<i>Mucositis:</i> Not defined <i>Peri-implantitis:</i> PPD > 5 mm, BoP/SUP & bone loss/level, no threshold	Not reported	Patient level: 23.7% Implant level: 13.3%	<i>Mucositis:</i> Estimated extent: 97% Severity: not reported <i>Peri-implantitis:</i> Estimated extent: 56% Severity: not reported
Ferreira et al. (2006)	Cross-sectional 0.5–5 years mean: 3.5 years	Brazil University Not reported	Convenience Initial: 212 Assessed: 212	Not reported	<i>Mucositis:</i> BoP & absence of bone loss <i>Peri-implantitis:</i> PPD ≥ 5 mm, BoP/SUP, & bone level, no threshold	Patient level: 64.6% Implant level: 62.6%	Patient level: 8.9% Implant level: 7.4%	<i>Mucositis:</i> Estimated extent: 97% Severity: not reported <i>Peri-implantitis:</i> Estimated extent: 83% Severity: not reported
Fransson et al. (2005, 2008, 2009, 2010)	Cross-sectional 5–20 years mean: 8.6 years	Sweden University Not reported	Convenience Initial: 662 Radiographic assessment: 662 Clinical assessment: 82	Not reported	<i>Mucositis:</i> BoP & bone loss ≤ 0.6 mm from year 1 <i>Peri-implantitis:</i> BoP & bone level ≥ 3 threads & bone loss > 0.6 mm from year 1 after loading	Implant level: $> 90\%$	Patient level: 27.8% Implant level: 12.4%	<i>Mucositis:</i> Not reported <i>Peri-implantitis:</i> Extent: 41.8% Severity: 32% of implants with bone loss ≥ 2 mm

Table 2. (continued)

First author, year	Study design & function time	Site, setting & funding	Sampling & sample size	Implant loss	Case definition	Prevalence of mucositis	Prevalence of peri-implantitis	Extent and severity of peri-implant diseases
Koldslund et al. (2010)	Cross-sectional 1–16 years mean: 8.4 years	Norway University Institutional	Convenience Initial: 164 Assessed: 109	Patient level: 9.2% Implant level: 4.8%	<i>Mucositis</i> : BoP/SUP & absence of bone loss <i>Peri-implantitis</i> : BoP/ SUP & bone loss >0.4 mm from loading	Patient level: 39.4% Implant level: 27.3%	Patient level: 47.1% Implant level: 36.6%	<i>Mucositis</i> : Estimated extent: 70% Severity: not reported <i>Peri-implantitis</i> : Estimated extent: 78% Severity (different case definitions): • PPD \geq 4 mm, BoP/ SUP & bone loss \geq 2 mm: 20.4% • PPD \geq 4 mm, BoP/SUP & bone loss \geq 3 mm: 11.7%
Marrone et al. (2013)	Cross-sectional 5–18 years mean: 8.5 years	Belgium Private & university Not reported	Convenience Initial: 112 Assessed: 103	Not reported	<i>Mucositis</i> : PPD \leq 5 mm, BoP & bone level \leq 2 mm <i>Peri-implantitis</i> : PPD > 5 mm, BoP & bone level > 2 mm	Patient level: 31% Implant level: 38%	Patient level: 37% Implant level: 23%	<i>Mucositis</i> : Estimated extent: 100% Severity: not reported <i>Peri-implantitis</i> : Estimated extent: 63% Severity: not reported
Máximo et al. (2008)	Cross-sectional \geq 1 year mean: 3.4 years	Brazil University Not reported	Convenience Initial: 224 Assessed: 113	Not reported	<i>Mucositis</i> : BoP & bone level $<$ 3 threads <i>Peri-implantitis</i> : PPD \geq 5 mm, BoP/SUP & bone level \geq 3 threads	Patient level: 36.3% Implant level: 32.0%	Patient level: 12.4% Implant level: 7.5%	<i>Mucositis</i> : Estimated extent: 88% Severity: not reported <i>Peri-implantitis</i> : Estimated extent: 61% Severity: not reported
Mir-Mari et al. (2012)	Cross-sectional 1–18 years mean: 6.3 years	Spain Private Institutional	Convenience Initial: 245 Assessed: 245	Not reported	<i>Mucositis</i> : BoP & bone level $<$ 2 threads <i>Peri-implantitis</i> : BoP/SUP & bone level \geq threads	Patient level: 38.8% Implant level: 21.6%	Patient level: 16.3% Implant level: 9.1%	<i>Mucositis</i> : Estimated extent: 55% Severity: not reported <i>Peri-implantitis</i> : Extent in patients with \geq 4 implants: 37% Severity: not reported

Table 2. (continued)

First author, year	Study design & function time	Site, setting & funding	Sampling & sample size	Implant loss	Case definition	Prevalence of mucositis	Prevalence of peri-implantitis	Extent and severity of peri-implant diseases
Roos-Jansäker et al. (2006)	Cross-sectional 9–14 years mean: 11.0 years	Sweden University Institutional	Convenience Initial: 294 Assessed: 216	Patient level: 10.1% Implant level: 4.4%	<i>Mucositis</i> : PPD ≥4 mm, BoP & bone level <1 thread <i>Peri-implantitis</i> : BoP/SUP & bone loss ≥1.8 mm from year 1 after loading	Patient level: 48% Implant level: 16%	Patient level: 16% Implant level: 6.6%	<i>Mucositis</i> : Estimated extent: 33% Severity (different case definitions): PPD ≥5 mm, BoP & bone level <1 thread: 16% PPD ≥6 mm, BoP & bone level <1 thread: 4% <i>Peri-implantitis</i> : Estimated extent: 41% Severity (different case definitions): BoP/SUP & bone loss >3 mm: 7.4% <i>Mucositis</i> : Not reported <i>Peri-implantitis</i> : Extent: 50% Severity: not reported
Zetterqvist et al. (2010)	RCT 5 years	Seven centers Europe & USA Private & university Industry	Convenience Initial: 112 Assessed: 96	Patient level: 0% Implant level: 0%	<i>Mucositis</i> : Not defined <i>Peri-implantitis</i> : PPD >5 mm, BoP/SUP & bone loss >5 mm from loading	Not reported	Patient level: 1% Implant level: 0.4%	

BoP, Bleeding on probing; PPD, Probing pocket depth; SUP, Suppuration.

Table 3. Quality of reporting: Adherence to Strobe checklist (included studies)

Strobe criteria	Casado et al. (2013b)	Cecchinato et al. (2013, 2014)	Dvorak et al. (2011)	Ferreira et al. (2006)	Fransson et al. (2005, 2008)	Koldslund et al. (2010)	Marrone et al. (2013)	Máximo et al. (2008)	Mir-Mari et al. (2012)	Roos-Jansäker et al. (2006)	Zetterqvist et al. (2010)
Title and abstract	1/2	2/2	2/2	1/2	1/2	1/2	1/2	1/2	2/2	1/2	2/2
Introduction	2/2	2/2	2/2	2/2	2/2	2/2	2/2	2/2	2/2	2/2	2/2
Methods	7/13	8/12	9/13	7/12	8/12	8/12	7/12	8/13	10/13	6/11	6/11
Results	5/8	6/9	4/8	6/10	5/8	7/5	8/8	6/10	3/8	4/7	5/8
Discussion	4/4	4/4	4/4	4/4	2/4	3/4	2/4	4/4	4/4	3/4	2/4
Other info	1/1	1/1	1/1	0/1	0/1	1/1	0/1	0/1	1/1	1/1	1/1
Adherence	67%	77%	73%	65%	62%	71%	55%	66%	73%	63%	64%

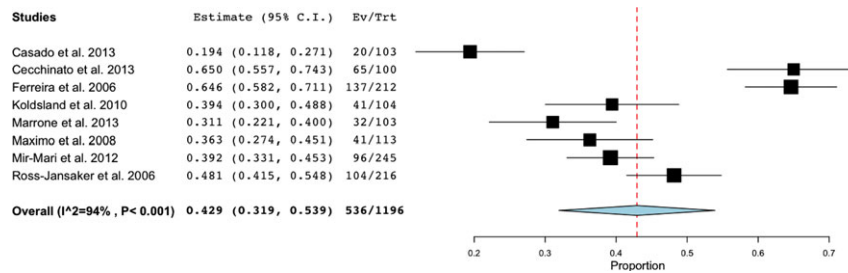


Fig. 2. Meta-analysis for prevalence of peri-implant mucositis.

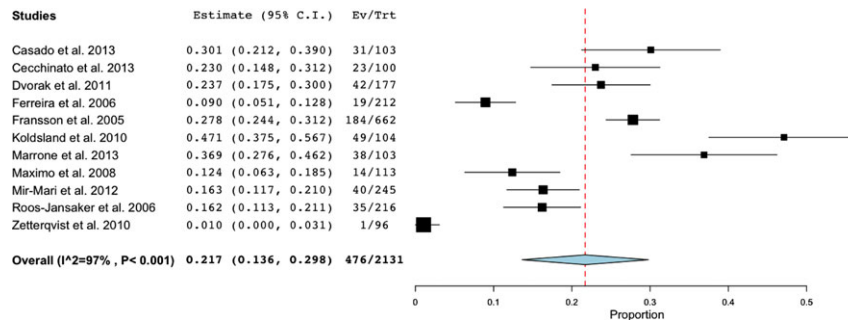


Fig. 3. Meta-analysis for prevalence of peri-implantitis.

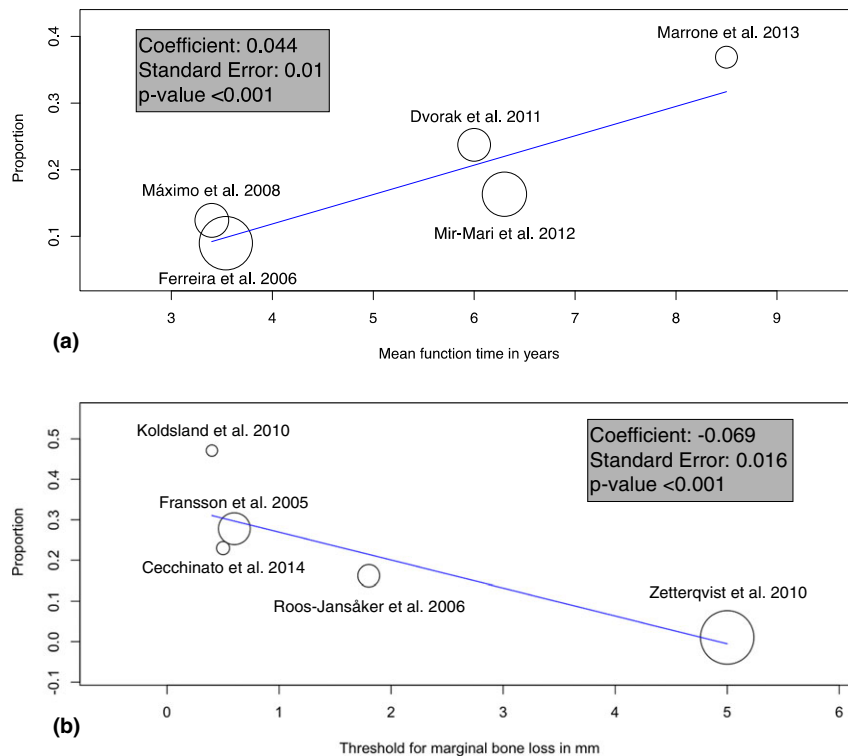


Fig. 4. (a) Meta-regression analysis for influence of function time on the prevalence of peri-implantitis (studies assessing bone levels of similar magnitude). (b) Meta-regression analysis for influence of bone loss threshold on the prevalence of peri-implantitis (studies assessing bone loss of varying magnitude).

Peri-implantitis

Two studies described the extent of peri-implantitis. Mir-Mari et al.

(2012) reported that in patients provided with ≥ 4 implants and diagnosed with peri-implantitis a total of

37% of all implants were affected. Fransson et al. (2009) reported an extent of 41.8%. The estimated

extent in the remaining studies ranged from 37–83%.

Information on severity of peri-implantitis could be extracted from four studies. Cecchinato et al. (2014) described an overall prevalence of peri-implantitis (PPD ≥ 4 mm, BoP & bone loss >0.5 mm) of 23%. The prevalence of subjects exhibiting peri-implantitis in combination with bone loss >1 mm and >2 mm was 16 and 7%, respectively.

Koldslund et al. (2010) and Roos-Jansåker et al. (2006) diagnosed peri-implantitis in 47 and 16% of all patients, respectively. Among these patients, a smaller number exhibited bone loss exceeding 3 mm (12 and 7%, respectively). Fransson et al. (2010) reported that 32% of all affected implants presented with a bone loss of ≥ 2 mm.

Discussion

The present systematic review highlighted some limitations of the available literature in regard to the prevalence, extent and severity of peri-implant diseases. All studies were based on convenience samples, mostly of limited size. The variety of case definitions used illustrated the lack of consensus in research.

The identified studies reported a prevalence of peri-implant mucositis ranging from 19 to 65%, while the prevalence of peri-implantitis ranged from 1 to 47%. Without disregarding the importance of case definition and time of follow-up, yet not including them in the meta-analyses, estimated weighted mean prevalences for peri-implant mucositis and peri-implantitis were 43% (95% CI: 32–54%) and 22% (95% CI: 14–30%), respectively. In contrast to disease, peri-implant health was not directly reported and could not be estimated from the presented data.

As no consensus exists on tools assessing the quality of observational studies (Lang & Kleijnen 2010), the STROBE checklist was used for evaluation of quality of reporting (Tomasi & Derks 2012). All studies fulfilled more than half of the suggested items. The majority of missing items were related to the description of material and methods as well as results. This finding suggests the need for more detailed description of methodology and results in future studies.

An obvious limitation of the included studies was related to the sampling procedure as all studies recruited convenience samples. Ideally, inferring the prevalence of a disease on a given population requires a randomly selected sample of adequate size. One inclusion criteria in the present review was a minimum sample size of 100 patients as suggested by Zitzmann & Berglundh (2008) at the 6th European Workshop on Periodontology. However, when comparing studies on peri-implant diseases to studies on periodontal diseases (e.g. Eke et al. 2012), it is obvious that the presently included studies are of rather limited size. As the present systematic review included assessments of peri-implantitis as well as peri-implant mucositis, no limit in regard to minimum function time was set for studies to be included.

Data originated primarily from university clinics. It should be noted, however, that four of the included studies (Zetterqvist et al. 2010, Mir-Mari et al. 2012, Cecchinato et al. 2013, 2014, Marrone et al. 2013) comprised patients treated in private clinics. Future studies should consider including randomly selected patients treated in different clinical settings by a multitude of clinicians.

While all included studies have applied the definitions for peri-implant diseases as previously suggested (Albrektsson & Isidor 1994, Zitzmann & Berglundh 2008), the case definitions used varied significantly in terms of thresholds for bone loss or bone levels. It is obvious that different disease thresholds have an impact on the rate of disease occurrence. In fact, the study (Zetterqvist et al. 2010) applying the highest threshold for bone loss (5 mm) when assessing peri-implantitis reported the lowest prevalence of peri-implantitis (1%). The study (Koldslund et al. 2010) with the lowest threshold for bone loss (0.4 mm) reported the highest prevalence (47%). Figure 4b further illustrates the relationship between disease thresholds and prevalence.

There is obvious need for consensus in terms of disease thresholds to facilitate comparisons. At the 8th European Workshop on Periodontology, Sanz & Chapple (2012) suggested case definitions for future epidemiological research to deter-

mine presence or absence of peri-implant diseases. For studies on prevalence, in the absence of baseline radiographs, a bone level of 2 mm from the expected level together with clinical inflammation was set as a threshold to define peri-implantitis. For studies on incidence of peri-implant diseases with existing baseline radiological measures, a bone loss of 1–1.5 mm in combination with inflammation was chosen. It should be noted that only few of the studies included in this review applied case definitions that were in line with the new recommendations (Bone level: Marrone et al. 2013, Bone loss: Cecchinato et al. 2013, 2014).

Zitzmann & Berglundh (2008) suggested that epidemiological research on peri-implant diseases should report not only on the prevalence or incidence of such but also on extent and severity. Extent, i.e. the number of affected implants in affected patients, was rarely directly reported (Fransson et al. 2009, Mir-Mari et al. 2012) as was the severity of peri-implant diseases (Roos-Jansåker et al. 2006, Fransson et al. 2010, Koldslund et al. 2010, Cecchinato et al. 2014). Future studies should apply case definitions suggested by consensus conferences (e.g. Sanz & Chapple 2012) and should furthermore describe severity, e.g. by grouping affected implants according to the degree of bone loss.

Longitudinal observations were rarely described as the majority of studies were of cross-sectional design, comprising a wide range of implant function time. Cross-sectional studies provide information on the prevalence of a disease, i.e. the number of cases at a given time point. Information on the incidence, i.e. the number of new cases in a given time period, however, may be obtained from prospective longitudinal studies. Such studies are difficult to perform. Similarly, studies describing epidemiology of periodontal diseases predominantly report prevalence rather than incidence data (e.g. Eke et al. 2012).

Only two studies described a mean function times of >10 years (Roos-Jansåker et al. 2006, Cecchinato et al. 2014). For several of the cross-sectional studies the minimum function time for inclusion was as

short as 12 months. Fransson et al. (2010) demonstrated that the rate of peri-implantitis associated bone loss was time-dependent. In addition, a meta-regression performed in the present review demonstrated a positive association between function time and the prevalence of peri-implantitis. Hence, it may be speculated that including patients with such short function time in studies on epidemiology of peri-implant diseases may result in underestimating the population prevalence.

Limitations of the performed meta-analyses are obvious. Heterogeneity across studies was high as indicated by I^2 (Peri-implant mucositis: 94%; Peri-implantitis: 97%). Risk of bias across studies was not assessed. Hence, the reported results should be interpreted with caution. The heterogeneity of case definitions, the variation in follow-up time and the selection of patients present in the currently available literature constitute a risk for incorrect estimation of the true prevalence of peri-implant diseases.

In conclusion, future studies on the epidemiology of peri-implant diseases should consider applying suggested case definitions (Sanz & Chapple 2012). Randomly selected patients should preferably be included and reasonable minimum function times should be considered. Reporting should include prevalence, extent and severity of the different disease entities.

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Clinical Relevance

Scientific rationale for the review: A wide range of data in regard to the prevalence of peri-implant diseases has been reported. The rationale of the present work was to summarize and analyse existing evidence.

Principal findings: The current systematic review illustrated that definitions for peri-implant mucositis and peri-implantitis varied significantly between available studies. Findings also indicated that peri-implant diseases are commonly occurring complications in implant therapy.

Practical implications: Clinicians should be aware of the risk of peri-implant diseases and should inform their patients prior to treatment. Clinical strategies should include preventive measures.

Appendix 1

Table A1. Checklist according to PRISMA statement

Section/topic	#	Checklist item	Adherence	Page
Title				
Title	1	Identify the report as a systematic review, meta-analysis, or both	Yes	1 & 2
Abstract				
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number	Partial	2
Introduction				
Rationale	3	Describe the rationale for the review in the context of what is already known	Yes	4
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	Yes	4 & 15
Methods				
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number	No	–
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale	Yes	5
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched	Yes	5
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated	Yes	15
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis)	Yes	5 & 20
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators	Yes	5 & 20
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made	Yes	5
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis	Partial	19

Table A1. (continued)

Section/topic	#	Checklist item	Adherence	Page
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means)	Yes	5
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis	Yes	6
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies)	No	—
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified	Yes	6
Results				
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram	Yes	20
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations	Yes	16–18
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12)	Yes	19
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot	Yes	16–18, 20–21
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency	Yes	20–21
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15)	No	—
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16])	Yes	21
Discussion				
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers)	Yes	10
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias)	Yes	12
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research	Yes	12
Funding				
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review	Yes	12

Table A2. Checklist according to STROBE Statement

	Item No	Recommendation
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract (b) Provide in the abstract an informative and balanced summary of what was done and what was found
Introduction		
Background/ rationale	2	Explain the scientific background and rationale for the investigation being reported
Objectives	3	State specific objectives, including any prespecified hypotheses
Methods		
Study design	4	Present key elements of study design early in the paper
Setting	5	Describe the setting locations and relevant dates, including periods of recruitment, exposure, follow up, and data collection
Participants	6	(a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow up <i>Case control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls <i>Cross sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants (b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed <i>Case-control study</i> —For matched studies, give matching criteria and number of controls per case
Variables	7	Clearly define all outcomes exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable

Table A2. (continued)

	Item No	Recommendation
Data sources/measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement)
Bias	9	Describe comparability of assessment methods if there is more than one group
Study size	10	Describe any effort to address potential sources of bias
Quantitative variables	11	Explain how the study size was arrived at
Statistical methods	12	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
		(a) Describe all statistical methods, including those used to control for confounding
		(b) Describe any methods used to examine subgroups and interactions
		(c) Explain how missing data were addressed
		(d) <i>Cohort study</i> —If applicable explain how loss to follow up was addressed
		<i>Case-control study</i> —If applicable explain how matching of cases and controls was addressed
		<i>Cross-sectional study</i> —If applicable describe, analytical methods taking account of sampling strategy
		(e) Describe any sensitivity analyses
Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—e.g., numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow up, and analysed
		(b) Give reasons for non-participation at each stage
		(c) Consider use of a flow diagram
Descriptive data	14*	(a) Give characteristics of study participants (e.g., demographic, clinical, social) and information on exposures and potential confounders
		(b) Indicate number of participants with missing data for each variable of interest
		(c) <i>Cohort study</i> —Summarise follow-up time (e.g., average and total amount)
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time
		<i>Case control study</i> —Report numbers in each exposure category, or summary measures of exposure
		<i>Cross-sectional study</i> —Report numbers of outcome events or summary measures
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g., 95% confidence interval) Make clear which confounders were adjusted for and why they were included
		(b) Report category boundaries when continuous variables were categorized
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analysis	17	Report other analysis done—e.g., analysis of subgroups and sensitivity analysis
Discussion		
Key results	18	Summarize key results with reference to study objectives
Limitations	19	Discuss limitations of study, taking into account sources of potential bias or imprecision
		Discuss both direction and magnitude of any potential bias
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies and other relevant evidence
Generalizability	21	Discuss the generalizability (external validity) of the study results
Other information		
Funding	22	Give the sources of funding and the role of the funders for the present study and, if applicable, for the original study for which the present article is based

Table A3. Reason for exclusion

First author, year	Study design & function time	Site, setting & funding	Sampling & sample size	Case definition	Reason for exclusion
Baelum & Ellegaard (2004)	Prospective case series 0–14 years	Denmark Private Not reported	Convenience Initial: 140 Assessed: 140	<i>Mucositis</i> : Not defined <i>Bone loss</i> : ≥1.5 mm or ≥3.5 mm	Lack of clear case definitions Data not reported on patient level
Behneke et al. (2002)	Prospective case series 5–8.7 years	Germany University Not reported	Convenience Initial: 100 Assessed: 83	<i>Mucositis</i> : Not defined <i>Bone loss</i> : > 3 mm	Lack of clear case definitions Data not reported on patient level
Casado et al. (2013a)	Cross-sectional 1–8 years	Brazil University Not reported	Convenience Initial: 215 Assessed: 215	<i>Mucositis</i> : BoP, absence of bone loss <i>Peri-implantitis</i> : BoP, bone loss (>1 mm + 0.2 mm × years of function)	Prevalence of mucositis and peri-implantitis not reported

Table A3. (continued)

First author, year	Study design & function time	Site, setting & funding	Sampling & sample size	Case definition	Reason for exclusion
Costa et al. (2012)	Prospective cohort study 5.5–10 years	Brazil University Institutional	Convenience Initial: 137 Assessed: 80	<i>Mucositis</i> : Visual inflammation & BoP, absence of bone loss <i>Peri-implantitis</i> : PPD \geq 5 mm, BoP/SUP, bone loss	Analysis of a subset of previously published data (Ferreira et al. 2006)
De Boever et al. (2009)	Prospective cohort study mean: 48 months	Belgium University Industry	Convenience Initial: 221 Assessed: 194	<i>Mucositis</i> : Not defined <i>Peri-implantitis</i> : Not defined	Lack of clear case definitions Data not reported on patient level
Gruica et al. (2004)	Prospective cohort study 8–15 years	Switzerland University Institutional & Industry	Convenience Initial: 223 Assessed 180	<i>Mucositis</i> : Not defined <i>Peri-implantitis</i> : Not defined	Lack of clear case definitions
Lopez-Piriz et al. (2012)	Cross-sectional 4–5 years	11 centers Spain Private Institutional	Convenience Initial: 147 Assessed 117	<i>Mucositis</i> : Not defined <i>Bone loss</i> : \geq 3 mm	Lack of clear case definitions Data not reported on patient level
Mangano et al. (2010)	Prospective case series 4 years	Six centers Italy Not reported Not reported	Convenience Initial: 295 Assessed 290	<i>Mucositis</i> : Not defined <i>Peri-implantitis</i> : Not defined	Lack of clear case definitions Data not reported on patient level
Roccuzzo et al. (2010, 2012)	Prospective cohort study 10 years	Italy Private Not reported	Convenience Initial: 112 Assessed: 101	<i>Mucositis</i> : Not defined <i>Bone loss</i> : \geq 3 mm	No data on mucositis and peri-implantitis
Roccuzzo et al. (2014)	Prospective cohort study 10 years	Italy Private Not reported	Convenience Initial: 149 Assessed: 123	<i>Mucositis</i> : Not defined <i>Bone loss</i> : \geq 3 mm	No data on mucositis and peri-implantitis
Stoker et al. (2012)	RCT 8 years	the Netherlands University Industry	Convenience Initial: 110 Assessed: 94	<i>Mucositis</i> : Not defined <i>Peri-implantitis</i> : Bone loss \geq 3 mm & PPD > 5 mm	Diagnosis not based on clinical signs of inflammation

BoP, Bleeding on probing; PPD, Probing pocket depth; SUP, Suppuration.