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SUPPLEMENT ARTICLE

WILEY CLINICAL ORAL IMPLANTS RESEARCH

How do peri-implant biologic parameters correspond with implant survival and peri-implantitis? A critical review

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Abstract

Objectives: The aim of this critical review was to evaluate whether commonly used biologic diagnostic parameters correspond to implant survival and peri-implantitis prevalence.

Materials and methods: Publications from 2011 to 2017 were selected by an electronic search using the Pubmed database of the US National Library of Medicine. Prospective and retrospective studies with a mean follow-up time of at least 5 years and reporting prevalence of peri-implantitis as well as mean bone loss and standard deviation were selected. The correlation between reported prevalence of peri-implantitis and reported implant survival, mean follow-up time, mean bone loss, mean probing depth, and mean bleeding on probing was calculated. Mean bone loss and standard deviation were used for estimation of proportion of implants with bone loss exceeding 1, 2, and 3 mm.

Results: Full-text analysis was performed for 255 papers from 4,173 available ones, and 41 met all the inclusion criteria. The overall mean weighted survival rate was 96.9% (89.9%–100%) and the reported prevalence of peri-implantitis ranged between 0% and 39.7%, based on 15 different case definitions. The overall weighted bone loss was 1.1 mm based on 8,182 implants and an average mean loading time ranging from 5 to 20 years. No correlation was found between mean bone loss and the reported prevalence of peri-implantitis. The estimated prevalence of implants with bone loss above 2 mm was 23%. The overall weighted mean probing depth was 3.3 mm, and mean weighted bleeding was 52.2%. Only a weak correlation was found between survival and function time ($r = -0.49$). There was no relation between the probing depth or bleeding and the mean bone loss, mean follow-up time, and reported prevalence of peri-implantitis.

Conclusion: Biologic parameters mean probing depth and mean bleeding on probing do not correlate with mean bone loss and this irrespective of follow-up. Case definition for peri-implantitis varied significantly between studies indicating that an unambiguous definition based on a specified threshold for bone loss is not agreed upon in the literature.

KEYWORDS

bone loss, diagnosis, implant success, implant survival, Peri-implantitis, review

1 | INTRODUCTION

Dental implants are widely used to restore partial and full edentulism. Due to a continuous improvement of implant designs, implant surface topographies, and prosthetic components, implant dentistry today yields excellent long-term results in terms of implant survival. Doornewaard et al. (2017) performed a systematic review including papers with above 5-year follow-up yielding a 97.3% weighted implant survival rate. Numerous clinical studies with a 10-year follow-up yield survival rates of over 95% (Buser et al., 2012; Degidi, Nardi & Piattelli, 2012; Fischer & Stenberg, 2012; Gotfredsen, 2012; Jemt, 2017). For single tooth replacements on turned implants, cumulative survival rates of 96.8% after 17–19 years (Bergenblock, Andersson, Furst & Jemt, 2012) and 91.5% after 16–22 years (Dierens, Vandeweghe, Kisch, Nilner & De Bruyn, 2012) were reported. In fully edentulous jaws, a 97% implant survival after on average 14 years has been reported (Vandeweghe, Ferreira, Vermeersch, Marien & De Bruyn, 2016). Up to 20 years, implant survival rates in the range of 80%–95% have been reported with turned implants in fully edentulous jaws (Astrand, Ahlqvist, Gunne & Nilson, 2008; Attard & Zarb, 2004; Ekelund, Lindquist, Carlsson & Jemt, 2003; Lindquist, Carlsson & Jemt, 1996). Chappuis et al. (2013) reported in a prospective study 89.5% survival of titanium plasma-sprayed implants after 20 years of function in partially edentulous cases. Compared with the era of introduction of dental implants in clinical practice half a century ago, implant survival is today predictable, regardless of implant length, implant diameter, bone quality, available bone volume, surgical, or prosthetic treatment protocol (Buser, Sennerby & De Bruyn, 2017). Apart from restoring function and esthetics, this has also affected patient-reported quality of life (De Bruyn, Raes, Matthys & Cosyn, 2015).

This positivity has over the last decade been affected by the escalating discussion on peri-implantitis, which has divided the scientific community and risks to ruin the good reputation of implant dentistry. Some of these disagreements are related to the inconsistency in the case definition, case selection, and the variability in diagnostic thresholds for disease (Albrektsson, Chrcanovic, Ostman & Sennerby, 2017; Coli, Christiaens, Sennerby & Bruyn, 2017; Derks & Tomasi, 2015). Two recent systematic reviews indicated that homogeneity in peri-implantitis reporting is still lacking. Tomasi and Derks (2012) listed nine different threshold levels for radiographic bone loss applied to diagnose peri-implantitis, and Ramanauskaite and Juodzbalys (2016) detected 10 case definitions for peri-implantitis. It is doubtful whether this is beneficial for the patient in the long run given the clinical treatment consequences that may follow, which could lead to unnecessary surgical treatment or even implant removal.

It is evident that patient-related factors such as the inability to perform oral hygiene are related to peri-implantitis (Serino & Strom, 2009), and regular maintenance is key for prevention (de Souza et al., 2013). This is confirmed by a meta-analysis including 13 papers concluding that a more regular, individually tailored peri-implant maintenance therapy prevents possible biologic complications over time and improves the long-term outcome of implants (Monje et al., 2016). Recent systematic reviews scrutinized additional patient-related factors and their association with implant treatment outcome. Among them, smoking habits have been shown to affect implant failure irrespective of implant surface, increase the risk of postoperative infection, and yield more marginal bone loss especially in the maxilla (Chrcanovic, Albrektsson & Wennerberg, 2015). The history of periodontal disease was suggested as a second important patient-related factor. An increased susceptibility for periodontitis may translate into an increased susceptibility for implant loss, loss of supporting bone, and/or postoperative infection (Chrcanovic, Albrektsson & Wennerberg, 2014). No significant relation could be identified between diabetes and implant failure as no differences were observed between patients with and without diabetes (Chrcanovic, Albrektsson & Wennerberg, 2014). As concluded in multiple articles, the difference in occlusal loading between immediate non-functional and immediate functional loading may not affect the survival of these implants and no significant effect on the marginal bone loss has been reported (Chrcanovic, Albrektsson & Wennerberg, 2014). Furthermore, peri-implant mucositis can also be induced by residual cement in the sulcus (Linkevicius et al., 2013) or be related to implant/prosthetic factors and lead to peri-implantitis (Pesce et al., 2015). In a systematic review including 79 papers (Doornewaard et al., 2017), it was suggested that the implant factor surface roughness had an impact on peri-implant bone loss. The bone loss around the moderately rough and minimally rough surface implants was less than around rough surface implants. The additional meta-analysis confirmed that a history of periodontal disease and smoking leads to more peri-implant bone loss.

1.1 | Definition of peri-implant disease

Peri-implant mucositis is defined by the 6th European Workshop of Periodontology as a reversible inflammation of the peri-implant soft tissue with no signs of loss of the supporting bone. In the 7th European Workshop, it was diagnosed as bleeding on gentle probing (Lang, Berglundh, & Working Group 4 of Seventh European Workshop on Periodontology, 2011). Peri-implantitis is defined as inflammation of the soft tissues in combination with ongoing loss of the supporting peri-implant bone beyond the physiological bone adaptation (Lindhe, Meyle, & Group D of European Workshop on Periodontology, 2008). The latter takes place as a consequence of biologic width establishment during initial healing. In the 3rd EAO consensus conference, it was stated that this initial bone remodeling may be unrelated to infection and is not necessarily peri-implantitis (Klinge, Meyle & Working, 2012). It was therefore suggested that monitoring of implant performance should not be based on radiographs taken after implant placement but should relate to baseline recordings once tissue homeostasis has been established, in essence 3 months after completion of the treatment (Klinge et al., 2012). Today, there is a general consensus that a baseline radiograph is required for the assessment of bone changes over time (Lang, et al., 2011). It is unfortunate that, this baseline radiograph is not always

available when clinicians assess the peri-implant tissue condition. For these conditions, a pragmatic clinical approach for peri-implantitis diagnosis was suggested by the 8th European Workshop for Periodontology (Sanz, Chapple, & Working Group 4 of the VIII European Workshop on Periodontology, 2012). The consensus report suggested a 2 mm additional loss beyond the "expected" bone level as a threshold in situations where baseline radiographic bone level assessment is lacking.

1.2 | Bone loss

Although the threshold for bone loss as a diagnostic criterion for disease is not exactly specified in the previous EFP or EAO consensus meetings, there is agreement on the fact that stable crestal bone levels are most important for implant success because it is paramount for long-term survival, esthetics, as well as peri-implant health. Klinge et al. (2012) advised that critical bone loss ≥2 mm from the time of placement of the prosthetic device, in combination with bleeding on probing, should be interpreted as a "red flag" for the clinician to critically evaluate whether any intervention is indicated in the individual case and whether follow-up and reassessment are required to confirm ongoing bone loss.

De Bruyn, Vandeweghe, Ruyffelaert, Cosyn and Sennerby (2013) reviewed radiographic assessment of modern implants and suggested that this mean bone loss assessment in patients with multiple implants yields very limited information on the condition of individual implants. However, it may be valid to benchmark implant systems. Given the fact that a majority of implants have very stable crestal bone levels over time and in a majority of cases sometimes no bone loss at all, the statistical interpretation of mean values often hides the condition of individual implants. It may be the reason why in the early studies, with mostly multiple implant cases for complete jaw rehabilitations, disease may have been overlooked. This is obvious from a radiographic follow-up study of 640 patients with 3,462 turned implants (Pikner, Grondahl, Jemt & Friberg, 2009). The mean bone loss after 5 years was 0.8 mm, and insignificant changes were reported in the years thereafter. However, the prevalence of implants with bone level located 3 mm apical to the implant–abutment junction was 2.8% at the time of prosthesis insertion but increased to 5.6%, 10.8%, 15.2%, 17.2%, and 23.5% after 1, 5, 10, 15, and 20 years, respectively. Vervaeke, Collaert, Cosyn and De Bruyn (2016) performed a prospective study, whereby 50 full-arch rehabilitations were immediately loaded the day of surgery on 5–8 implants in the maxilla and mandible and followed for 9 years. Implant survival was 99.2%, and the total mean bone loss, including initial remodeling, was calculated on patient level being limited to 1.7 mm. However, on implant level, 30% of the individual implants had lost more than 2 mm, figures largely affected by the inclusion of smokers and patients with a periodontal history. Hence, in the context of peri-implantitis, the mean crestal bone values calculated on patient level are not appropriate to detect disease around individual implants. The same holds true for cross-sectional evaluation at a given time point when the baseline radiograph is lacking and bone levels are used as surrogate for peri-implantitis detection. A recent report of Pettersson and Sennerby (2015) revealed that 15% of the implants showed more than 2 mm bone loss after 5 years. Applying the criteria of Sanz, et al. (2012), these implants could be diagnosed with peri-implantitis. However, in this particular study, 25% of the implants had already bone loss up to 2 mm due to the specific implant design and over time there was stability or even improvement of the bone level.

1.3 | Probing depth

Periodontal probing is a common basic diagnostic tool in periodontal diagnosis around teeth. Ericsson and Lindhe (1993) had described distinct differences between teeth and implants in soft tissue composition, organization, and attachment between the gingiva and the root surface on one hand and between the peri-implant mucosa and the implant surface on the other. Therefore, this affects the interpretation of probing depth measurements. In healthy tissue, the probe penetration is more advanced around implants (Eickholz, Grotkamp, Steveling, Muhling & Staehle, 2001; Ericsson, 1986; Klinge, 1991) although this is depending on the probing force (Lang, Wetzel, Stich & Caffesse, 1994). Soft tissue around implants has also been found thicker than around teeth. This was first described in animals (Berglundh et al., 1991) and confirmed by human biopsies (Tomasi et al., 2014). Parpaiola et al. (2015) assessed the dimensions of the soft tissue cuff present at various aspects around teeth and implants using human biopsies. The soft tissue cuff that surrounded a tooth varied between 2 mm at flat surfaces and 4 mm at proximal surfaces, while at implant sites, the mucosa at proximal as well as flat surfaces was 1–1.5 mm greater. The probing depth (PD) was greater at proximal than at facial or palatal/lingual surfaces at tooth sites and frequently also at implant sites. Furthermore, the PD and the soft tissue thickness were greater at implant than at adjacent tooth sites. Another study (Choquet et al., 2001) confirmed soft tissue thickness ranging between 0.85 mm and 6.85 mm and papilla heights of 7 mm to 9 mm under healthy conditions. Kan, Rungcharassaeng, Umezu and Kois (2003) measured an average interproximal thickness of the mucosa of 6 mm with a large range. Gallucci, Belser, Bernard and Magne (2004) found mesial and distal PD often ranging between 4 and 8 mm depending on how scalloped the mucosa is. Animal studies have shown that conditions of mild inflammation already yield deeper pockets around implants compared to teeth and this does not necessarily coincide with actual bone loss (Schou et al., 2002). A multilevel analysis performed in a group of 52 patients with screw-retained restorations on 92 implants revealed that deeper PD is associated with higher tendency to bleed. This would indicate that an increase in PD in the absence of additional bone loss may be indicative of peri-implant mucositis (Klinge, 1991). Also, Lang et al. (1994) concluded that the probe penetrates into the connective tissue in situations of mucositis. A few studies have looked for correlations between bone loss and clinical parameters among them probing. They concluded that probing depths are of limited value in predicting future peri-implant bone loss (Dierens et al., 2012; Giannopoulou,

Bernard, Buser, Carrel & Belser, 2003; Weber, Crohin & Fiorellini, 2000). Long-term clinical studies have clearly shown that the probing depth of healthy peri-implant mucosa is not always smaller than 4 mm but very often up to 6 mm (Dierens et al., 2012; Karoussis et al., 2004; Lekholm et al., 1986). In an 18-year follow-up of single turned implants, pockets of up to 9 mm were found despite the absence of bone loss (Bergenblock et al., 2012). Also, Dierens et al. (2012) could not demonstrate correlations between PD and marginal bone levels around single implants functional for 16–22 years. Deep (>5 mm) and shallow (<4 mm) pockets were found in all bone level groups explaining the poor predictive value of probing in the peri-implantitis diagnosis when based on bone loss alone.

Probing is hindered by the location of the implant restoration especially in case of partial or full jaw reconstructions. This may be the reason while in some studies patients with multiple implant cases are diagnosed more often with peri-implantitis. Dalago, Schuldt Filho, Rodrigues, Renvert and Bianchini (2017) speculated that this could be attributed to less adequate oral hygiene or possible inclusion of more patients with periodontal history. Also, Serino and Strom (2009) proved that 65% of the implants with no good accessibility for oral hygiene showed peri-implantitis compared to 18% when oral hygiene was feasible. It is obvious that incorrect probing may lead to iatrogenic bleeding. De Bruyn, Bouvry, et al. (2013) evaluated full jaw patients with implants placed in onlay grafts in the maxilla after a mean follow-up of more than 9 years. To assess the peri-implant health, they removed the screw-retained reconstruction; 11% of the implants presented with a PD ≥ 5 mm despite more than 39% of the implants with BoP. There was no correlation between the registered BoP 39% and the bone loss, but the PD reflected the bone loss. Serino, Turri and Lang (2013) demonstrated differences in PD with or without the implant construction in place. The PD showed a high correlation with bone loss when the reconstruction was removed. The presence of the construction impeded the accuracy of the PD registration, and only in 37% of the sites, similar results were obtained with probing with or without the construction. They concluded that PD reflects the bony defect only when access for probing is ideal. However, full jaw prosthesis often present with overhang, which may lead to inaccurate probing and false-positive diagnosis. In addition, the measurement error encountered with probing is higher around implants than around teeth (Eickholz et al., 2001; Mombelli, Muhle, Bragger, Lang & Burgin, 1997), and the type of implant may affect the absolute PD value.

The aforementioned studies all suggest that the use of an absolute PD threshold to diagnose the soft tissue around implants should be performed with great caution. Based on the current evidence, the PD value alone cannot be considered a reliable indicator for defining peri-implantitis (Serino et al., 2013). When actual bone loss is not correctly taken into account, due to the absence of a baseline radiograph, and when the PD is the only determining factor in the diagnosis, this may undoubtedly account for the high reported prevalence of peri-implantitis in some studies. It is obvious that change in PD over time, once a physiological steady state in the soft tissue has been established, may be regarded as an indicator of disease activity. Huang et al. (2013) suggested that a baseline PD should be established as a basis for comparison over time because initial implant location may affect the PD. A recent systematic review (Lee, Huang, Zhu & Weltman, 2017) concluded that the use of progressively deepening probing depth is more meaningful than using absolute PD values of ≥4 or 5 mm.

1.4 | Bleeding on probing

Bleeding on probing is used in periodontal diagnosis. It is a poor predictor of disease progression, but the absence of BoP is a good predictor of future tissue stability (Lang, Adler, Joss & Nyman, 1990). Lekholm et al. (1986) reported that neither deep pockets nor BoP was found to be accompanied by accelerated marginal bone loss. The probability of a peri-implant site to bleed upon probing is associated with PD, implant position and gender (Farina, Filippi, Brazzioli, Tomasi & Trombelli, 2017). Jepsen, Ruhling, Jepsen, Ohlenbusch and Albers (1996) found no difference in BoP between sites with progressive bone loss or stable sites. They pointed out that probing might also provoke a nonspecific bleeding that is unrelated to the amount of inflammation and most probably related to the presence of the microgap between implants and abutments or reconstruction. Indeed, studies comparing teeth and implants, with respect to soft tissue healing, revealed that peri-implant healing as determined by crevicular molecular composition differs from periodontal healing. It is suggested that peri-implant tissues represent a higher pro-inflammatory state (Emecen-Huja et al., 2013). An analysis of 987 implants followed for 9–14 years demonstrates that signs of mucositis (BoP) are evenly distributed among implants with or without peri-implantitis. There was actually no difference in the proportion of implants with the absence or presence of bleeding/suppuration in relation to bone loss, bone gain, or bone stability (Roos-Jansaker, Lindahl, Renvert & Renvert, 2006). Another large cohort study, including 4,591 implants from 2,060 subjects, indicated that minimal bleeding did not correlate with bone loss but multipoint bleeding, profuse bleeding, or suppuration did (French, Cochran & Ofec, 2016). The use of a dichotomous diagnostic criterion (bleeding yes or no) is probably the reason why often high figures of mucositis are reported. Dierens et al. (2012) revealed 80% of BoP-positive implants after 16–22 years of follow-up despite a prevalence of peri-implantitis as low as 5% and found no correlation between BoP and peri-implantitis. Renvert, Lindahl and Persson (2018) evaluated 86 individuals at an examination after 9–14 years and furthermore after 21–26 years of function; 58% of the individuals with no bone loss during the interval had been diagnosed with mucositis during the first examination. On the other hand, nearly 22% of the patients without any sign of mucositis after 9–14 years had developed peri-implantitis at a later stage. Data analysis failed to show that a diagnosis of mucositis after 9–14 years was predictive for development of peri-implantitis after 21–26 years. This recent paper is in contradiction with the suggestion of Jepsen et al. (2015) that mucositis is a precursor for peri-implantitis. This contradiction does not imply that one should

TABLE 1 The number of papers and summarized relevant clinical information

Article number	Author (year)	Study design	Treatment subgroups	Mean follow-up years (range)	Patients baseline	Implants baseline	Survival %	Implants for BL follow-up
1	Shi et al. (2018)	R		10.1 (8–14.6)	67	98	96.6	95
2a	Sener-Yamaner et al. (2017)	P	1: early loaded SLA	6.8	55	107	99.0	106
2b			2: early loaded SLA-active	6.8		68	97.0	66
3	Galindo-Moreno et al. (2017)	P		5	69	97	95.9	93
4a	den Hartog et al. (2017)	P	1: smooth neck	5	31	31	96.2	26
4b			2: rough neck	5	31	31	100	28
4c			3: scalloped rough neck	5	31	31	96.2	26
5	Froum and Khouly (2017)	R		8.5	52	52	100	28
6a	Ayna, Gulses and Acil (2018)	P	1: all-on-four mandible metal ceramic	7	16	64	100	60
6b			2: all-on-four mandible bar retained	7	16	64	100	64
7a	Taschieri et al. (2017)	R	1a: P-PRP immediate loading	5	71	30	97.5	11
7b			1b: P-PRP delayed loading	5		49		28
7c			2a: non-P-PRP immediate loading	5	38	11	97.9	9
7d			2b: non-P-PRP delayed loading	5		37		10
8	Cassetta et al. (2016)	P		5	270	576	94.1	542
9	Ekfeldt et al. (2017)	R		10.5 (10–11)	23	30	100	30
10	Jensen et al. (2017)	R		8 (3–16)	26	52	91.7	43
11	Tey et al. (2017)	R		5.9	194	266	100	266
12	Cosyn et al. (2016)	P		5	22	22	95.0	17
13	Glibert, De Bruyn and Ostman (2016)	P		6.2 (5.4–6.9)	40	112	99.1	111
14	Derks et al. (2016)[a]	R		8.9	596	2367	97.0	1578
15a	Sanchez-Siles et al. (2015)	R	1: smooth neck	6.44	171	515	100	515
15b			2: without smooth neck	5.61	229	729	100	729
16	Donati, Ekestubbe, Lindhe and Wennstrom (2016)	P		12	40	45	97.0	35

Time of baseline radiograph	Mean implant BL in mm (SD)	Info on PPD	Mean PPD (mm)	Bleeding index used	Bleeding score %	Reported suppuration	Reported PI prevalence % on implant level	Definition of PI
1	1.19 (1.07)	Mean	3.7	BoP	33.4	No	8.5	11
0	0.71 (0.35)					No	1.0	X
	0.53 (0.28)					No	3.0	
0	0.15 (0.95)	0.20 mm PPD reduction		BoP	57.5	No	0.0	X
0	1.26 (0.90)	Mean	3.5	BoP	79.2	No	7.7	11
	1.20 (1.10)	Mean	3.3	BoP	59.3	No	14.2	
	2.28 (0.97)	Mean	4.3	BoP	87.5	No	11.5	
0	0.30 (0.73)	Mean	2.2	BoP	53.6	No	3.6	3
0	0.74 (0.17)	Mean	3.3	BoP	18.8	No	0.0	X
	0.76 (0.15)	Mean	3.6	BoP	32.8	No	0.0	
0	0.8 (0.35)					No	3.8	6
	1.02 (0.27)					No		
	0.6 (0.16)					No	10.4	
	0.8 (0.89)					No		
1	0.59 (1.34)					No	4.9	X
1	0.26 (0.60)	30% PPD > 4 mm		BoP	13.0	No	13.0	5 with cutoff bone loss of 0.6 mm
0	0.9 (1.0)	Mean	3.3	mBI = 0.7		No	8.7	5 with cutoff bone loss of 2mm
9	1.05 (1.07)	Fd: 7.1% PPD ≥ 6 mm		BoP	95.0	No	7.1	3
0	0.19 (0.30)	Mean	3.1	BoP	32.0	No	0.0	X
0	0.35 (0.45)					No	0.9	11
1	0.72 (1.15)	16.9% PPD ≥ 6 mm		BoP	60.9	No	24.9	15
9	1.12 (1.24)			Only for implants with PI		Yes	2.9	5
	2.51 (1.57)			Only for implants with PI		Yes	14.4	
1	0.61 (2.10)			BoP	25.0	No	8.6	11

(Continues)

Article number	Author (year)	Study design	Treatment subgroups	Mean follow-up years (range)	Patients baseline	Implants baseline	Survival %	Implants for BL follow-up
17a	Canullo et al. (2016)	P	1: steam cleaning abutment	5	15	15	100	15
17b			2: plasma of argon cleaning abutment	5	15	15	100	15
18	Vandeweghe et al. (2016)	R		14.3 (10–21)	33	203	97.0	197
19	Nedir, Nurdin, Vazquez, Abi Najm and Bischof (2016)	P		10	17	25	100	23
20	van Velzen et al. (2015)	P		10	250	506	99.7	367
21	Trullenque-Eriksson and Guisado-Moya (2014)	R		13.19 (8.46–24.37)	105	342	90.6	342
22	Meijer et al. (2014)	P		10	150	240	95.3	240
23	Schropp, Wenzel and Stavropoulos (2014)	P		10	63	63		47
24	Mangano, Iaculli, Piattelli and Mangano (2015)	R		15.2 (10–20)	49	178	97.2	178
25	Simion, Gionso, Grossi, Briguglio and Fontana (2015)	R		12	29	59	93.2	59
26	Meyle et al. (2014)	P		10	20	54	96.3	54
27	Anitua, Pinas, Begona and Orive (2014)	R		10.3 (7.2–11.4)	75	111	98.9	87
28	Donati et al. (2015)	P		5	151	161	95.6	140
29	Gelb, McAllister, Nummikoski and Del Fabbro (2013)	R		7.33 (7–8)	57	107	100	107
30	Chappuis et al. (2013)	R		20	67	95	89.5	85
31a	Renvert et al. (2012)	R	1: TiOblast	13	27	132		80
31b			2: TiUnite	13	27	102		84
32	Frisch et al. (2013)	R		14.1 (10.2–18.9)	22	89	98.9	89
33	Lops et al. (2012)	P		13.2 (10–21)	121	257	92.3	207
34	Ormianer et al. (2012)	R		10	46	173	99.4	172
35a	Ravald, Dahlgren, Teiwik and Grondahl (2013)	P	1: TiOblast	13.5 (12–15)	66	184	95.0	136
35b			2: Machined	13.5 (12–15)	66	187	94.7	116
36	Ostman et al. (2012)	P		10	46	121	99.2	106
37a	Arnhart et al. (2013)	R	1: TiUnite	6.7 (5.3–9.8)	47	136	98.5	136
37b			2: Machined	8.2 (5.3–9.8)		52	96.2	52
38	Lai et al. (2013)	R		10	168	231	98.3	231

TABLE 1 The number of papers and summarized relevant clinical information(Continued)

Time of baseline radiograph	Mean implant BL in mm (SD)	Info on PPD	Mean PPD (mm)	Bleeding index used	Bleeding score %	Reported suppuration	Reported PI prevalence % on implant level	Definition of PI
1	0.65 (0.36)			BoP	6.6	No	0.0	X
	0.21 (0.21)			BoP	20.0	No	0.0	
0	1.73 (1.54)	Mean	3.6	BoP	47.2	No	4.1	3
0	1.00 (0.90)					Yes	8.7	X
0	1.21 (0.94)	Mean	3.7	BoP	52.5	No	7.0	10
1	1.84 (1.35)					No	1.7	13
1	1.10 (1.10)	Mean	3.4	mBI = 0.3		No	20.3	11
0	0.67 (0.98)	Fd: 36% PPD ≥ 5 mm		BoP	70.0	No	4.3	9
1	1.80 (0.60)					Yes	2.3	12
1	1.34 (0.79)	Mean	2.9	BoP	54.7	No	0.0	8
1	0.60 (0.26)	Mean	3.3	BoP	27.0	No	23.8	5
0	0.95 (0.65)					Yes	0.9	X
0	0.32 (1.15)	Fd: 3.2% PPD ≥ 6 mm		BoP	13.0	No	2.9	11
0	1.49 (1.03)			BoP	4.7	No	0.0	X
0	0.14 (1.09)	Mean	3.1	sBI = 0.1		Yes	20.0	X
1	0.80 (–)	Mean	2.6	BoP	82.1	Yes	32.1	Four with cutoff bone loss of 1mm
	1.0 (–)	Mean	3.1	BoP	89.7	Yes	39.1	
1	1.80 (1.50	Mean	3.1	BoP	21.0	No	8.0	1 with PPD ≥ 5 mm and BoP
1	1.85 (1.55)	Mean	2.2			No	8.7	X
9	0.18 (–)					No	2.3	X
0	0.70 (–)	Fd: 19% PPD ≥ 6 mm upper jaw and 11% PPD ≥ 6 mm lower jaw				Yes	6.0	X
	0.40 (–)	Fd: 3% PPD ≥ 6 mm upper jaw and 4% PPD ≥ 6 mm lower jaw				Yes	5.0	
0	0.70 (1.35)			BoP	9.2	Yes	1.9	4
1	1.53 (0.25)	Mean	3.1	BoP	76.8	No	0.0	X
	2.42 (0.34)	Mean	2.9	BoP	23.2	No	1.9	
0	0.63 (0.68)					No	2.0	14

(Continues)

Article number	Author (year)	Study design	Treatment subgroups	Mean follow-up years (range)	Patients baseline	Implants baseline	Survival %	Implants for BL follow-up
39	Levine, Sendi and Bornstein (2012)	P		5	20	21	100	21
40a	Rodrigo, Martin and Sanz (2012)	P	1: immediate placement	5	22	34		26
40b			2: delayed placement	5		34		26
41a	Roccuzzo, Bonino, Aglietta and Dalmasso (2012)	P	1: periodontally healthy	10	112	61	96.6	59
41b			2: moderately periodontally compromised	10	112	95	92.7	88
41c			3: severely periodontally compromised	10	112	90	90.0	81

BL, bone loss; PI, peri-implantitis; IL, immediate loading; DL, delayed loading; IP, immediate placement; DP, delayed placement; R, retrospective; P, prospective; mBI, mean bleeding index; sBI, sulcus bleeding index; BoP, bleeding on probing; Fd, frequency distribution; PPD, probing pocket depth.
Time of baseline radiograph: 0 after surgery 1; variable time point after loading; 9 unknown.
[a]In the Derks paper, only implants with bone loss data were extracted. Definition of peri-implantitis: refer to Table 2.

become negligent and should not strive for the prevention of mucositis with good oral hygiene.

1.5 | Prevalence of peri-implantitis

The prevalence of peri-implant diseases significantly varies among clinical studies due to the inconsistent definitions, reporting methods and study characteristics. One of the first publications on the prevalence of peri-implant diseases by Zitzmann and Berglundh (2008) based on only two cross-sectional studies reported 28–77% on patient level and 12–43% on implant sites with peri-implantitis. Mombelli, Muller and Cionca (2012) calculated the prevalence of peri-implantitis, based on 29 papers, in the order of 10% of the affected implants and 20% patients during 5–10 years after implant placement. Another review summarizing 10 papers reporting on the 10-year clinical outcome with implants treated by sandblasting, grit blasting, acid-etching, or combined treatments revealed that the survival was above 95% and <5% were diagnosed with purulent infection or peri-implantitis (Albrektsson, Buser & Sennerby, 2012). A 10-year follow-up study including nearly 300 implants in 100 subjects revealed similar figures (Cecchinato, Parpaiola & Lindhe, 2014). They concluded that implant sites with radiographically confirmed marginal bone loss of ≥1 mm were not common and that peri-implantitis defined as bone loss >0.5 mm, BoP^{+}, and PD ≥ 6 mm was detected in 12% of patients and only 5% of implants. Atieh, Alsabeeha, Faggion and Duncan (2013) performed a systematic review including information of 1,497 patient with 6,283 implants and reported a respective prevalence of 18.8% on patient level and 9.6% on implant level. Derks and Tomasi (2015) performed a systematic review including 11 clinical studies and reported a broad range in the prevalence of peri-implant mucositis (19%–65%) and peri-implantitis (1%–47%). The meta-analyses estimated a weighted mean prevalence of peri-implantitis affecting 22% of the implants. The meta-regression showed a positive relationship between prevalence of peri-implantitis and function time. This report was critically appraised by Jemt, Karouni, Abitbol, Zouiten and Antoun (2017) mentioning that the broad range in the prevalence could be attained to different thresholds for bone loss (range 0.4 mm–5 mm) used in the various case definition applied in the selected papers, in combination with a high dropout rate and the use of bone levels at a cross-sectional time point instead of absolute bone loss. The systematic review of Lee et al. (2017) included 47 studies whereby the bone level thresholds for disease ranged from 1 to 5 mm and lead to a weighted mean implant-based and subject-based peri-implantitis of 9.2% and 19.8%, respectively.

1.6 | Aim

The aim of this critical review was to describe whether the commonly used biologic diagnostic parameters correspond to long-term outcome in terms of implant survival and reported peri-implantitis prevalence.

2 | MATERIAL AND METHODS

2.1 | Search strategy

The focus of this study was on diagnostic aspects in relation to peri-implant health and clinical outcome in long-term perspective. Given

TABLE 1 The number of papers and summarized relevant clinical information(Continued)

Time of baseline radiograph	Mean implant BL in mm (SD)	Info on PPD	Mean PPD (mm)	Bleeding index used	Bleeding score %	Reported suppuration	Reported PI prevalence % on implant level	Definition of PI
0	0.58 (–)					No	0.0	X
1	2.20 (0.90)	Fd: 2.5% PPD ≥ 5 mm		BoP	14.2	No	8.8	7
	2.10 (1.00)	Fd: 0% PPD ≥ 5 mm		BoP	13.7	No	2.9	
0	0.75 (0.88)	Mean	3.1	BoP	12.0	No	4.7	2
	1.14 (1.11)	Mean	3.5	BoP	31.0	No	11.2	
	0.98 (1.22)	Mean	3.9	BoP	30.9	No	15.1	

the overall consensus that progressive bone loss is the most important biologic parameter in the diagnosis of peri-implantitis, it was decided to conduct a broad literature search using Pubmed database of the US National Library of Medicine for articles. Publications from 2011 up to September 2017 were selected using the general search algorithm: ((((((“bone loss”) OR “peri-implantitis”)) OR “periimplant”)) AND dental implant). Cross-sectional reports were excluded because they report on bone levels and not on bone loss. The papers had to be published in English, report on peri-implantitis prevalence together with mean bone loss on implant level (compared to a baseline measurement). No distinction was made based on study design (prospective or retrospective, RCT, or case series) or surgical or prosthetic treatment protocol as long as they included at least 10 patients after a minimal mean follow-up time of 5 years. Only studies discussing implant treatment in systemically healthy patients were included, but studies with smokers, patients with periodontal history, controlled diabetes, or implants in sinus lifted bone were allowed. Studies describing implant treatment in tumor-resected areas, studies involving extensive bone grafts or zygomatic or mini-implant were excluded. An independent selection was performed based on the title and detailed information given in the abstract by two assessors (RD & HDB) who discussed jointly and reached a consensus in case of disagreement over the inclusion/exclusion of a paper.

2.2 | Data analysis

Papers were descriptively analyzed, and case definitions of peri-implantitis were extracted. Analysis was performed on implant level. In the overall statistical analysis of implant survival and bone loss, the number of implants was used to weight the study or study groups throughout this review. A bivariate correlation analysis was performed using the Pearson r correlation coefficient. A correlation coefficient ranging from 0.01–0.19, 0.20–0.29, 0.30–0.39, 0.40–0.69, and above 0.70 represent a negligible, weak, moderate, strong, and very strong relationship, respectively. Correlation was calculated between the outcomes (i) reported prevalence of peri-implantitis and (ii) mean implant survival, mean time in function, mean bone loss, mean PD, and mean BoP. Based on studies reporting on skewness and distributions it could be expected that data, most commonly, are not normally distributed. This is caused by outliers, which could lead to large standard deviations, rather caused by chance than population. Therefore, the standard deviations on population level are not used in weighing of studies. The variability between studies is more reduced due to the lesser effect of outliers on the mean compared to the effect on the standard deviation and the amount of studies. Therefore, the Pearson correlation coefficients calculated, chosen as measure for a linear relationship between measures, are exploratory and could only be descriptively interpreted in conjunction with the graphical representations. If papers mentioned multiple case definitions, the one with the smallest bone loss threshold was applied in the correlation analysis. Papers with incomplete data reporting were not used for these analyses. In addition, the proportion of implants with bone loss above 1, 2, and 3 mm was estimated based on reported means and standard deviations. If the paper gave a frequency distribution for bone loss, the outcome of the frequency distribution was compared with the calculated proportion of implants with bone loss above 2 mm. Descriptive statistics were performed using MatLab R2015b version (8.6.0.267246; The MathWorks, Inc., Natick, MA, USA).

3 | RESULTS

3.1 | Selection and data reporting

The search yielded 4.173 papers whereof 255 publications were selected for full article reading. At last, 41 fulfilled the inclusion criteria, and the extracted data are summarized in Table 1. The peri-implantitis case definitions applied in the respective articles are illustrated in Table 2. In total, 41 articles, 21 prospective and 20 retrospective, report on 56 treatment groups. They represent in total 4,198 patients initially treated with 9,657 implants of various brands and with a variety of treatment protocols. A total of 6,246 implants were retrospectively analyzed, and 3,411 implants were prospectively analyzed. Table 3 shows the number of papers and their respective reported parameters.

3.2 | Survival rate and follow-up time

Thirty-eight of the 41 papers reported on survival rate in 49 treatment groups. The overall weighted mean survival rate was 96.9% [89.5%–100%] and 97.2% and 96.2% for retrospective and prospective studies, respectively. In 39 and nine treatment groups, the reported implant survival rate was ranging between 95.0%–100% and 90.0%–94.9%, respectively. Only one treatment group reported an implant survival below 90%. The weighted mean follow-up time for the 56 treatment groups was 9.0 years with a range of 3–24.4 years. The weighted mean follow-up was 9.2 (3–24.4) and 8.7 (5–21) years for retrospective and prospective groups, respectively. Thirty of the 56 treatment groups, representing initially 5886 implants, had a follow-up time between 5 and 9.9 years with 4,894 implants at follow-up (dropout 16.9%). In total, 24 treatment groups had a mean follow-up time ranging between 10 and 14.9 years, with 3,498 implants at baseline and 3,025 implants at follow-up (dropout 13.5%). Only two treatment groups had a mean follow-up time of 15 years or longer, with 273 implants at baseline and 263 at follow-up (dropout rate of 3.7%).

3.3 | Reported prevalence and case definition of peri-implantitis

For all the included 56 treatment groups, the prevalence of peri-implantitis on implant level ranged between 0% and 39.7% as shown in Table 1 and was based on 15 different case definitions of peri-implantitis. The case definitions varied considerably, mostly due to heterogeneous thresholds for bone loss and ranging from any detectable bone loss to 3.5 mm. Of the 41 papers, only 27 had a clearly defined threshold for bone loss, most commonly 2 mm. Some authors (Derks et al., 2015; Donati et al., 2015; Tey, Phillips & Tan, 2017) used more than one threshold and also gave more than one prevalence. Tey et al. (2017) made a distinction between clinical peri-implant disease definitions according to Pjetursson et al. (2012) and the prevalence of peri-implantitis based on radiographic diagnosis. Derks et al. (2015) used a combination of BoP and/or suppuration with a bone loss threshold of 0.5 mm and diagnosed 24.9% with peri-implantitis. However, when they used a bone loss threshold of 2.0 mm, only 7.8% of the implants were diagnosed with peri-implantitis. Also, Donati et al. (2015) used two different bone loss thresholds. Peri-implantitis was diagnosed in 2.9% or 5.7% of the implants when applying 2 or 1 mm thresholds for bone loss, respectively. The highest prevalence of peri-implantitis (although coined incidence in the paper) was found in the study by Renvert, Lindahl and Rutger Persson (2012), originally reporting on 234 implants of two different brands after 7 years of function in 54 patients. After 13 years, 164 implants were available for radiographic evaluation, which resulted in a dropout rate of 29.9% on implant level. The mean bone loss for the two study groups was 0.8 mm and 1.0 mm, respectively. Peri-implantitis was detected in nearly 40% of the implants based on a bone loss threshold above 1 mm following the first year after implant placement.

3.4 | Mean bone loss

The weighted overall mean bone loss as reported in the papers was 1.1 mm (SD 1.0) and 1.3 mm (SD 1.1) and 0.9 mm (SD 1.0) for the retrospective and prospective studies, respectively. Time point of baseline radiographs was inconsistent. Baseline radiographs for bone loss calculation were taken immediately after implant placement in 22 papers, several months after the placement in 15 papers and three papers did not provide information about the time point. Figure 1 summarizes the mean bone loss in relation to the follow-up time. With the reported mean and standard deviation, the estimation of the proportion of implants with cutoff bone loss above 1, 2, and 3 mm was calculated per treatment group and amounted to 51%, 23%, and 8%, respectively (Figure 2).

3.5 | Mean peri-implant probing depth and bleeding scores

In 25 papers, representing 34 treatment groups, the mean peri-implant probing depth was reported. The overall mean weighted PD was 3.3 mm; 75% of the treatment groups reported a mean PD between 3.0 and 3.9 mm and only one treatment group reported a mean PD above 4 mm, whereas the majority of papers reported the mean PD, four papers gave a detailed frequency distribution as can be seen in Table 4. Twenty-eight of the 41 included papers (38/56 treatment groups) reported mean bleeding scores around implants using various indices. Twenty-four papers (34/56 treatment groups) reported mean peri-implant bleeding on probing with a weighted mean of 52.2%, ranging from 4.7% to 95.0%. The BoP around implants was <25% for 13 treatment groups, ranging from 25% to 49.9% for eight treatment groups and ranging from 50% to 74.9% for six treatment groups. In seven treatment groups, a BoP ≥ 75% was reported. Two papers reported the modified bleeding index (Mombelli, van Oosten, Schurch & Land, 1987): one the Sulcus bleeding (Muhlemann & Son, 1971) and one

TABLE 2 Overview of the different definitions for peri-implantitis used in the retrieved papers. The article number refers to the reference provided in Table 1

Definition number	References	Definition of peri-implantitis	Cutoff bone loss (mm)	Cutoff PPD (mm)	BoP/Sup	Frequency distribution of definition	Article number
1	Albrektsson, Zarb, Worthington and Eriksson (1986)	Bone loss 1.5 mm for the first year and 0.2 mm annually thereafter	1.5			1	32
2	Albrektsson and Isidor (1994): 1st EWOP	Inflammatory reactions associated with loss of supporting bone around an implant in function			BoP	1	41
3	Berglundh et al. (2002)	PPD > 6 mm in combination with bleeding on probing/suppuration and attachment loss/bone loss of 2.5 mm	2.5		BoP/Sup	3	5, 11, 18
4	Lindhe, et al. (2008): 6th EWOP	A mucosal lesion often associated with suppuration and deepened pockets, but always accompanied by loss of supporting marginal bone			BoP/Sup	2	31, 36
5	Lang, et al. (2011): 7th EWOP	Changes in the level of the crestal bone in conjunction with bleeding on probing with or without concomitant deepening of peri-implant pockets. Pus is a common finding in peri-implantitis sites.			BoP	4	9, 10, 15, 26
6	Self-reported definition 1	Inflammatory lesion in the peri-implant mucosa, associated with plaque, BoP and radiographic evidence of bone loss at mesial or distal aspect of implants			BoP	1	7
7	Self-reported definition 2	Significance bone loss, PPD ≥ 4 mm and BoP		4	BoP	1	40
8	Self-reported definition 3	Crater-like bone defect, PPD ≥ 4 mm and BoP/Sup		4	BoP/Sup	1	25
9	Self-reported definition 4	Bone loss > 1mm, PPD ≥ 5 mm and BoP/Sup	1	5	BoP/Sup	1	23
10	Self-reported definition 5	Bone loss >1.5 mm and BoP	1.5		BoP	1	20
11	Self-reported definition 6	Bone loss >2 mm and BoP/Sup	2		BoP/Sup	6	1, 4, 16, 22, 28
12	Self-reported definition 7	Bone loss ≥2.5 mm, PPD ≥ 6 mm, profuse bleeding/suppuration and pain	2.5	6	BoP/Sup	1	24
13	Self-reported definition 8	Bone loss >3 mm, PPD >5 mm and BoP/Sup	3	5	BoP/Sup	1	21
14	Self-reported definition 9	PPD > 6 mm and BoP/Sup		6	BoP/Sup	1	38
15	Self-reported definition 10	1) Bone loss >0.5 mm and BoP 2) moderate/severe = bone loss >2 mm and BoP	0.5 or 2		BoP	1	14

TABLE 3 Number of papers and the respectively reported clinical parameters

Clinical Parameter	Number of papers
Bone loss (BL)	41
Survival rate (SR)	38
Bleeding (B)	28
Probing pocket depth (PPD)	25
Suppuration (S)	8
Bone loss, survival rate and B + PPD + S	1
Bone loss, survival rate and two of the three parameters	21
Bone loss, survival rate and one of the three parameter	8
Bone loss and survival rate	8
Bone loss and B + PPD + S	1
Bone loss and two of the three parameters	2

gave only information about bleeding for implants diagnosed with peri-implantitis.

3.6 | Suppuration

Eight papers (Table 5) reported that 0%–20% of the implants showed suppuration independently from BoP. In four papers, this percentage corresponds nicely with the reported prevalence of peri-implantitis (~10%–40%), but in the other four papers, it did not. The high prevalence of 20% in the paper of Chappuis et al. (2013) is explained by the inclusion of six previously lost implants as well as 13 successfully treated ones.

3.7 | Correlation between reported prevalence of peri-implantitis and biologic parameters

Figures 3–5 report the Pearson r correlation coefficient, visualize the correlation between the different biologic parameters, and reported prevalence of peri-implantitis and follow-up time. The dimension of the different bullets in the figures reflects the weight of the study.

Figure 3 visualizes mean bone loss versus the reported peri-implantitis prevalence, the mean PD, and mean BoP quoted in the selected studies. The treatment group with the highest weight, being 1,578 implants (Derks et al., 2016), reported a prevalence of 25% with a mean bone loss of 0.7 mm, 61% of the implants showing BoP, and 17% of the implants with a PPD ≥ 6 mm. The smallest treatment group included 15 implants (Canullo et al., 2016) and detected no peri-implantitis with a limited mean bone loss (0.2 mm) and 20% of the implants showing BoP. Overall, the reported peri-implantitis prevalence (Figure 3a) was in the majority of studies lower than 10%. There was no distinct correlation between mean bone loss and peri-implantitis prevalence. The range of mean bone loss up to 2.5 mm may explain the large range in reported prevalence from 0% up to approximately 40%. The highest prevalence of nearly 40% was presented by Renvert et al. (2012), despite a mean bone loss of 1 mm after an average 13 years of follow-up. However, they defined peri-implantitis using a threshold for bone loss of 1 mm. Arnhart et al. (2013) reported a prevalence of only 2% with a much higher mean bone loss of 2.4 mm, but they did not define a threshold for bone loss. In addition, data suggested the absence of a distinct relationship between the biologic factors mean PD and mean BoP with mean bone loss. Some studies reported a high mean bone loss despite lower percentages of bleeding on probing. den Hartog, Meijer, Vissink and Raghoebar (2017) reported a mean bone loss of 2.3 mm after a follow-up of 5-year with a corresponding 87.5% BoP. Arnhart et al. (2013) gave a comparable mean bone loss of 2.4 mm after 8.2 years with only 23.2% BoP. Tey et al. (2017) reported the highest mean BoP score of 95% with a mean bone loss of only 1 mm and 7.1% of implants demonstrated peri-implantitis. On the other hand, mean BoP showed a large range (4.7%–95%) irrespective of mean bone loss or mean PD (Figure 3c).

Figures 4a,b illustrate the lack of a relationship between the reported prevalence of peri-implantitis and mean PD or mean BoP. Froum and Khouly (2017) reported the lowest mean PD (2.2 mm) and a corresponding reported prevalence of peri-implantitis of 3.6%. den Hartog et al. (2017) reported the highest mean PPD (4.3 mm) and a reported prevalence of peri-implantitis of 11.5%. Mean BoP showed a strong correlation with peri-implantitis (Pearson $r = 0.45$). Tey et al. (2017) reported 95% BoP with only 7.1% of the implants demonstrating peri-implantitis. Renvert et al. (2012) reported a similar 90% BoP with a mean PD of 3 mm but nevertheless 39% peri-implantitis. Another Swedish report (Ostman, Hellman & Sennerby, 2012) came up with 9% of BoP and only 2% of peri-implantitis, but PD values were missing.

Figure 5 visualizes the parameters survival rate, mean PD, and mean BoP in correlation with the mean function time. The survival rate shows negative strong correlation with the mean function time (Pearson $r = -0.49$). The correlation between mean PD and mean function time is weak (Pearson $r = -0.27$). There is no indication of correlation between the mean function time and mean BoP (Pearson $r = -0.06$).

4 | DISCUSSION

This review focused on reported peri-implantitis prevalence and diagnostic parameters considered important for long-term outcome. Biologic complications often coined as peri-implantitis may cause patient discomfort and may result in implant failure. For the current critical review, the search was limited from 2011 to September 2017, which coincides with the scientific debate on peri-implantitis. It was decided to include all types of studies to be as inclusive as possible. This may better reflect daily clinical practice when compared to well-controlled academic studies. Because peri-implantitis occurs commonly after longer function time, studies were included when at least 5 years of mean follow-up was reported. Over the last decade, there has been a tremendous increase in the use of dental implants

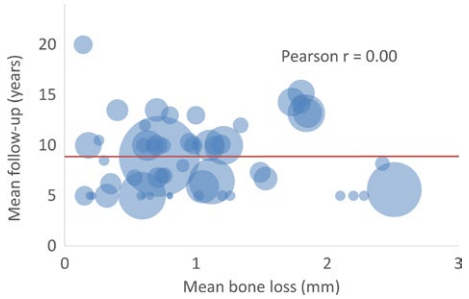

FIGURE 1 Mean bone loss (mm) in relation to the mean follow-up time (years) of the treatment groups; the size of the bullets reflects the number of implants reported in the treatment group

in daily clinical practice and consequently also scientific interest has increased. In 2011, twice as many papers appeared compared to 2006 and from 2011 until 2017 as many papers appeared than in the previous 35 years as visualized in Figure 6. Despite 4,173 initially selected papers, only 255 were selected for full reading and only 41 withstood the quality check. This is a disappointingly low proportion for a topic with such a significant impact for patients, clinicians, and implants industry.

The included material in this paper is strongly skewed toward retrospective studies, with 6,246 retrospective and 3,411 prospective analyzed implants. One could address that this leads to a higher inclusion of lower quality data. The high amount of retrospective included implants is mainly caused by the large study of Derks et al. (2016) with 2,367 implants at baseline. However, the results showed a similar survival rate for retrospective and prospective analyzed implants, 97.2% and 96.2%, respectively, and in view of the large standard deviation, the difference in overall mean weighted bone loss between retrospective and prospective studies is not conclusive. Due to the large heterogeneity in the definition of peri-implantitis, it was not possible to calculate whether there was a difference in the reported peri-implantitis prevalence between retrospective and prospective analyzed implants.

Regarding the statistical analysis, it was opted to use the Pearson correlation coefficient. Although the justification of this correlation coefficient instead of the Spearman's relation coefficient could be a point of debate when data are possibly not normally distributed, the distribution at the level of the separate studies is most often skewed, when reported, and the presence of outliers cannot be excluded. This results in the distinct difference in variability of the different studies and the unreliability of estimates of the standard deviation for the individual studies. To circumvent the problem of unreliable estimates of the standard deviation, weighting by sample size was performed. At the level of the studies, though, no real outliers are present. The Pearson correlation coefficient is a measure of linear approximation, and the Spearman correlation coefficient is a measure of association that is not immediately translates to linearity. In view of the attempt to demonstrate the absence or presence of linear relations, the Pearson correlation was chosen together with the graphical representation to visually assess the relation described by the coefficient. Testing of the correlation coefficient would have required normality at both levels and reliable estimates of the within variability and between study variability. It is clear that, these requirements were not met, and therefore, the presented results are exploratory and descriptive in nature.

The overall weighted mean implant survival in the selected studies was 96.9% based on remaining implants at the time of evaluation. This shows that dental implant treatment today can be considered predictable. Few papers report on implant failure caused by peri-implantitis alone. In five treatment groups (Arnhart et al., 2013; Cassetta, Driver, Brandetti & Calasso, 2016; Sener-Yamaner, Yamaner, Sertgoz, Canakci & Ozcan, 2017), 5%, 1%, 3%, 0%, and 2% of the implants were lost due to peri-implantitis. Sener-Yamaner et al. (2017) reported peri-implantitis related failures after 5 years of loading especially in smokers. Arnhart et al. (2013) mentioned the loss of two implants after 5 and 10 years because of peri-implantitis. The aforementioned three papers did not report prevalence of peri-implantitis for the remaining implants and were therefore excluded from the current review. Only two studies reported the prevalence

TABLE 4 Frequency distribution op probing pocket depth (mm), between brackets percentage of implants with BoP. The article number refers to the reference provided in Table 1

Article number	Author (year)	Treatment groups	Percentage probing pocket depth (% implants BoP)				
			≤3 mm	3.1–4 mm	4.1–5 mm	5.1–6 mm	>6 mm
11	Tey et al. (2017)		39.5 (89.5)	38.3 (99)	15.0 (95)	4.1 (100)	3.0 (100)
16	Donati et al. (2015)		80	16.8			3.2
35a	Ravald et al. (2013)	TiOblast upper jaw	49	32			19
		TiOblast lower jaw	66	23			11
35b		Machined upper jaw	47	50			3
		Machined lower jaw	70	26			4
40a	Rodrigo et al. (2012)	Immediate placement	82.9	14.2	2.4	0.5	
40b		Delayed placement	81.1	15.6	2.4	0.9	

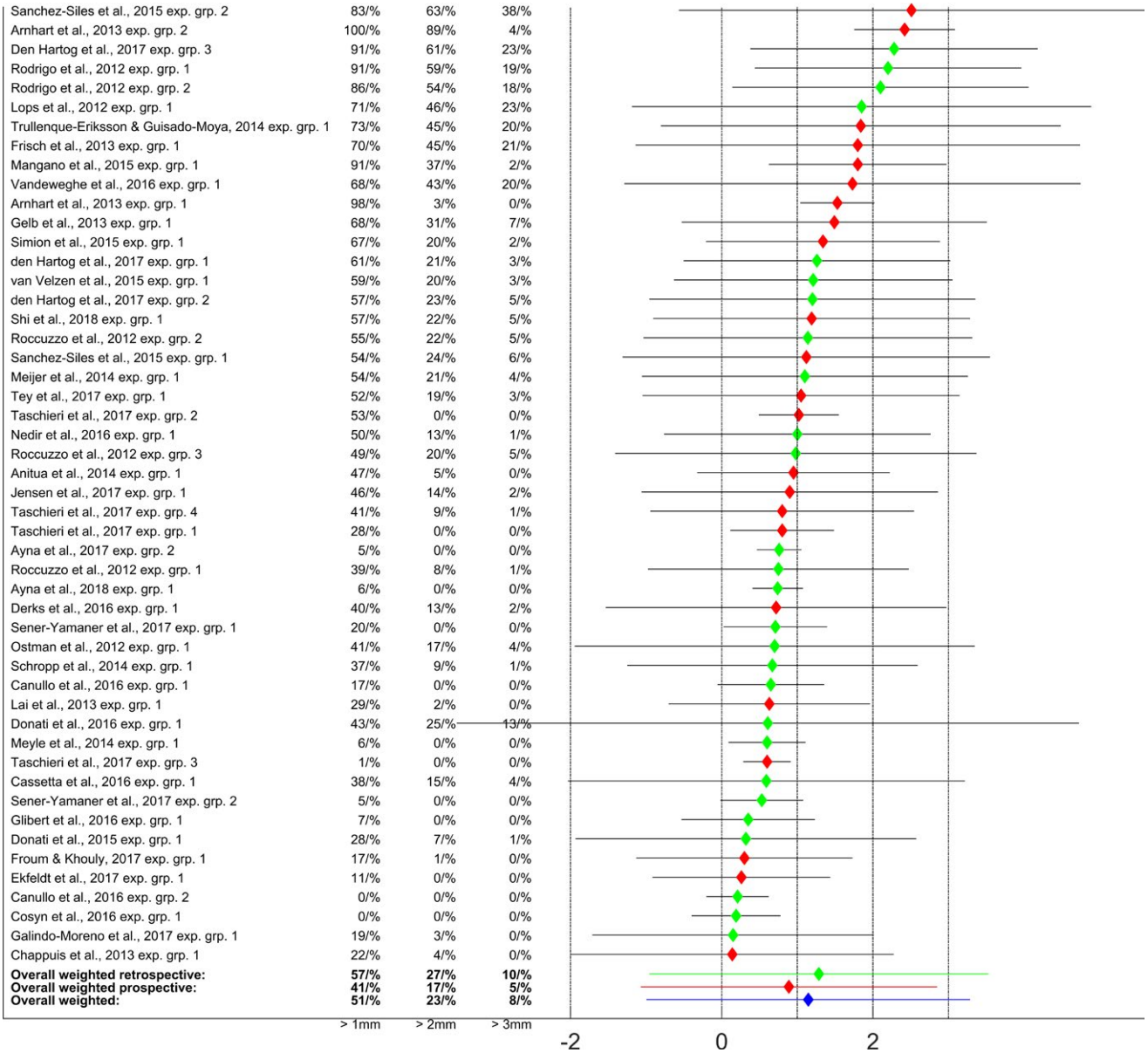

FIGURE 2 Mean bone loss (mm) per treatment group and estimated proportion of implants with bone loss above 1, 2, and 3 mm. (green = retrospective study design; red = prospective study design)

for peri-implantitis of both lost and functioning implants. Lops et al. (2012) described eight of 257 (3.1%) implants with mobility due to severe peri-implantitis and ten other implants were successfully treated during the 20-year follow-up period. Chappuis et al. (2013) reported 19 of 95 implants (20%) with peri-implantitis whereof six implants were lost and 13 underwent a successful anti-infectious therapy and were maintained with no further signs of acute infection. Both studies included the treated peri-implantitis implants in the reported prevalence figures despite successful treatment. In the other 36 papers, prevalence of peri-implantitis was related to surviving implants and dropouts or lost implants prior to the moment of assessment are not taken into account. One can conclude that information of peri-implantitis in lost implants is scarce, and hence, the reported prevalence may be underestimated in the available literature.

In this review, the prevalence of peri-implantitis on implant level ranged between 0% and 40%. The case definitions varied considerably between studies, mostly due to heterogeneous thresholds for bone loss, ranging from any detectable bone loss to 3.5 mm. This makes comparisons between studies difficult. Reflecting on the results presented in Table 6, it is obvious that reported prevalence figures are larger when the threshold is low. Using the same implant design, Swedish studies that applied a threshold bone loss of approximately 0.5 mm concluded that 13%–25% of the implants were affected (Derks et al., 2016; Ekfeldt, Furst & Carlsson, 2017). Thresholds of bone loss of 2–3 mm yield much lower prevalence in the order of 5%–10%. However, the paper of Meijer, Raghoebar, de Waal and Vissink (2014) seems contradictory in this respect. With a 2 mm threshold, they detected 20% despite a mean bone loss limited

TABLE 5 Suppurating implants (%) in relation to the reported peri-implantitis prevalence. The article number refers to the reference provided in Table 1

Article number	Author (year)	Treatment group	Suppurating implants/total number (%)	Reported PI prevalence on implant level (%)
15	Sanchez-Siles et al. (2015)		2/1244 (0.2)	9.6
19	Nedir et al. (2016)		0/25 (0.0)	8.7
24	Mangano et al. (2015)		4/178 (2.2)	2.3
27	Anitua et al. (2014)		1/111 (0.9)	0.9
30	Chappuis et al. (2013)		19/95 (20)	20.0
31a	Renvert et al. (2012)	1: TiOblast	(1.2)	32.1
31b		2: TiUnite	(3.8)	39.1
35a	Ravald et al. (2013)	1: TiOblast	2/136 (1.5)	6.0
35b		2: Machined	2/116 (1.7)	5.0
36	Ostman et al. (2012)		2/106 (1.9)	1.9

to 1 mm. Their material consisted of IMZ and TPS implants from the first generation, known to be prone to bone loss over time. Meyle, Gersok, Boedeker and Gonzales (2014) reported a similarly high prevalence of 24% but a low mean bone loss of 0.60 mm also after 10 years. The threshold of bone loss for the diagnosis for peri-implantitis was any bone loss and this could explain the high reported prevalence. If one were to apply the guidelines of the 8th European Workshop on Periodontology on their material, the prevalence would not be 23.8% but 0%. Also, Renvert et al. (2012) reported peri-implantitis prevalence of 32.1% and 39.7% for both treatment groups, respectively. The implants evaluated after 13 years showed a mean bone loss of 0.8 mm for TiOblast surfaces and 1.0 mm for TiUnite surfaces of peri-implantitis in both treatment groups. Despite this low mean bone loss, high bleedings scores around the implants of 82% and 90% were reported.

A serious problem in this review is the heterogeneity of the data and the variation of the follow-up time within each study. This was recognized by previous authors (Frisch, Ziebolz & Rinke, 2013; Trullenque-Eriksson & Guisado-Moya, 2014) and obvious from the study of Jensen, Meijer, Raghoebar, Kerdijk and Cune (2017). The latter had a mean follow-up time of 8 years based on implants in function from 3 years up to 16 years of follow-up. One could debate whether it is appropriate to sample implants with a large range in function time as being one group or whether cohort analysis based on function periods would be more justified.

Bone loss is in most of the studies expressed as a mean value with a standard deviation, which may hide outliers in the analysis. When reporting mean values of bone loss in a study population, it implies that the data are normally distributed. If this were the case, the mean and standard deviation would suffice to estimate the percentage of implants with a defined bone loss. Doornewaard et al. (2017) applied this in a systematic review and calculated the proportion of implants with bone loss over 1, 2 and 3 mm, respectively. The same approach was applied as a post hoc analysis using the 13 papers that reported both the mean and standard deviation and also

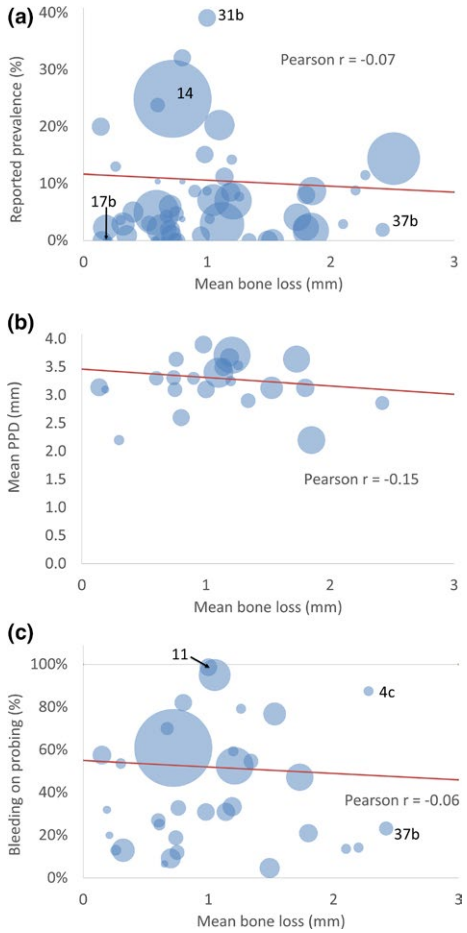

FIGURE 3 (a) Mean bone loss (mm) in relation to the reported prevalence of peri-implantitis (%); $r = -0.07$ (negligible correlation). (b) Mean bone loss (mm) in relation to probing pocket depth (mm); $r = -0.15$ (negligible correlation). (C) Mean bone loss (mm) in relation to bleeding on probing (%): $r = -0.06$ (negligible correlation); the size of the bullets reflects the number of implants reported in the treatment group; the number in the bullets refers to the article number provided in Table 1

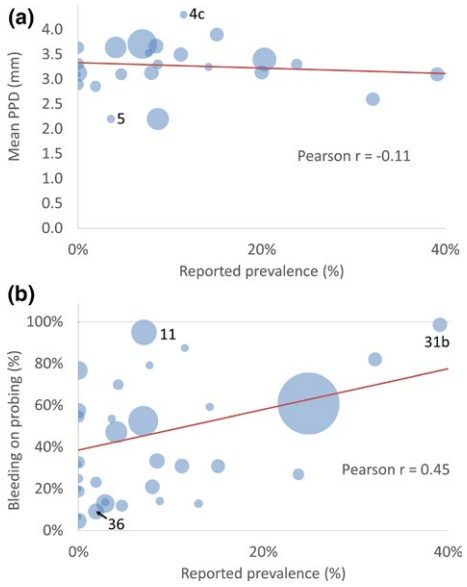

FIGURE 4 (a) Reported prevalence of peri-implantitis (%) in relation to mean probing pocket depth (mm): $r = -0.11$ (negligible correlation). (b) Reported prevalence of peri-implantitis (%) in relation to bleeding on probing (%): $r = 0.45$ (strong correlation); the size of the bullets reflects the number of implants reported in the treatment group; the number in the bullets refers to the article number provided in Table 1

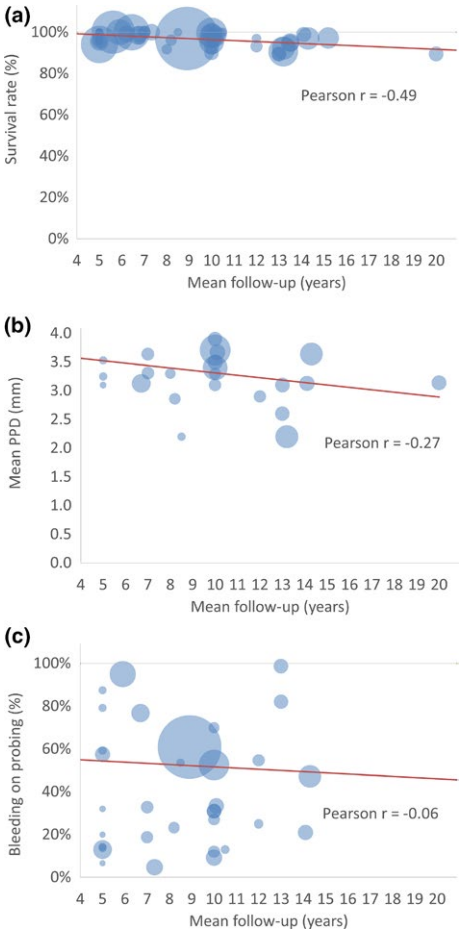

FIGURE 5 (a) Mean follow-up time (years) in relation to survival rate (%): $r = 0.49$ (strong correlation). (b) Mean follow-up time (years) in relation to probing pocket depth (mm): $r = -0.27$ (weak correlation). (c) Mean follow-up time (years) in relation to bleeding on probing (%): $r = -0.06$ (negligible correlation); the size of the bullets reflects the number of implants reported in the treatment group

gave a frequency distribution of bone loss as presented in Table 6. We observed that the calculated proportion of implants with bone loss was an overestimation when compared to the frequency distribution reported. Hence, bone loss is probably not normally distributed within the study population but positively skewed. Hence, nonparametric statistics is appropriate including statistical parameters median, interquartile ranges as well as frequency distributions. This could refine the prevalence figures in scientific reports. Only four of the 13 previously mentioned papers reported their data in this proposed way (Donati et al., 2015; Ekfeldt et al., 2017; Frisch et al., 2013; van Velzen, Ofec, Schulten & Ten Bruggenkate, 2015) and all reported lower medians than means. This may suggest that few implants with an extensive bone loss have a big impact on the mean and the standard deviation. This is confirmed by Donati et al. (2015) who detected three of the 35 evaluated implants with bone loss of 5, 7, and 9 mm. They reported a median of 0.2 mm and an interquartile range of −0.7 to 0.5 mm. Ekfeldt et al. (2017) showed comparable results where only two of the 30 evaluated implants lost, respectively, 1.8 mm and 2.4 mm bone. This resulted in a higher mean bone loss of 0.26 mm compared to a median of 0.0 mm. It is obvious that the methodology applied in our review yielded overestimated proportions of implants with a certain threshold of bone loss.

The pooled data from this review did not demonstrate a relationship between mean function time and mean implant survival or peri-implantitis prevalence. This could be partially explained by dropouts of implants that are not further assessed during follow-up.

This review contains four papers that reported the Kaplan–Meier survival analysis. Chappuis et al. (2013) reported a sudden increase after 12 years, the latter related to a combination of biologic and technical failures. Jensen et al. (2017) analyzed the implants retrospectively with a start of the measurement after 3 years and reported all losses before 5 years. Also, the other two papers showed

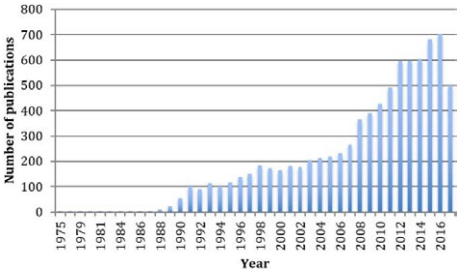

FIGURE 6 Number of publications per year from the search string applied in this systematic review

TABLE 6 Overview of studies giving a frequency distribution for implants with bone loss >2 mm in relation to prevalence of peri-implantitis and cutoff bone loss. The article number refers to the reference provided in Table 1

Article number	Author (year)	Mean bone loss (SD)	% Implants with estimated bone loss>2 mm based on given mean and SD (%)	Frequency distribution of implants with bone loss >2 mm as reported in the paper (%)	Reported prevalence of peri-implantitis (%)	Cutoff bone loss (mm)
1	Shi et al. (2018)	1.19 (1.07)	22	8.5	8.5	2
4a	den Hartog et al. (2017)	1.26 (0.90)	21	17.3	7.7	–
4b		1.20 (1.10)	23	16.	14.2	–
4c		2.28 (0.97)	61	64.0	11.5	–
8	Cassetta et al. (2016)	0.59 (1.34)	15	13.3	4.9	–
9	Ekfeldt et al. (2017)	0.26 (0.60)	0	3.33	13.0	0.6
11	Tey et al. (2017)	1.05 (1.07)	19	18.0	7.1	2.5
14	Derks et al. (2016)	0.72 (1.15)	13	9.9	24.9	0.5
16	Donati et al. (2015)	0.61 (2.10)	25	9.0	8.6	2
20	van Velzen et al. (2015)	1.21 (0.94)	20	5.99	7.0	1.5
22	Meijer et al. (2014)	1.10 (1.10)	21	16.0	20.3	2
25	Simion et al. (2015)	1.34 (0.79)	20	10.0	0.0	–
30	Chappuis et al. (2013)	0.14 (1.09)	4	0.0	20.0	–
32	Frisch et al. (2013)	1.80 (1.50)	45	35.0	8.0	3.5
36	Ostman et al. (2012)	0.70 (1.35)	17	11.3	1.90	–

a downhill Kaplan–Meier survival rate in relation to follow-up time (Meyle et al., 2014; Shi et al., 2018). It seems therefore appropriate to conclude that implants do fail over time, although in small numbers.

The mean PD reported in 25 of the 41 papers varied between 2.2 mm and 4.3 mm, with only one study reporting a mean PD above 4 mm. It is obvious from the results presented in this review that a relationship between mean PD and mean bone loss or peri-implantitis prevalence is absent. From a clinical perspective, one should realize that probing is technique sensitive and may be affected by probing force, probing direction, design of the restorations and design of implant, and type of prosthetic components. Obviously, the prosthetic reconstruction may jeopardize probing due to incorrect probing direction or restorations' overhangs. This may potentially also provoke iatrogenic bleeding. Serino et al. (2013) examined the PD before and after removal of the prosthetic reconstruction. While the PD before removal had a poor correlation with bone loss, it correlated well with the PD after removal as assessed during surgery. Christiaens et al. (2017) concluded that probing depth around peri-implantitis affected implants significantly underestimated the true bone level by 1 mm. Garcia-Garcia, Mir-Mari, Benic, Figueiredo and Valmaseda-Castellon (2016) showed a significant underestimation of the interproximal bone level by intra-oral radiography of 1.3 mm on average. Merli et al. (2014) concluded that assessment of bone loss by three clinicians showed the highest intraclass correlation coefficient while the intraclass correlation coefficient for PD and BoP was low. The paper of Coli et al. (2017) concluded, based on evidence from animal as well as human studies, that it is unreliable to simply diagnose an implant as having peri-implantitis because of a pre-established PD. It is well known that values of 6–9 mm PD have been described in association with long-term successful dental implants. Human studies have shown that in healthy peri-implant mucosa, the probing depths are in most of the cases (60%–63%) above 4 mm and even up to 6 mm (Bergenblock et al., 2012; Lekholm et al., 1986). One should also keep in mind that the interproximal probing depth measurement is affected by a significant papilla regrowth after crown installation. These findings support the importance of a combination of diagnostic parameters when diagnosing peri-implantitis.

This critical review revealed mean BoP ranging from 4.7%–95%. Gerber, Tan, Balmer, Salvi and Lang (2009) concluded that BoP is highly dependent on the probing pressure, which strengthens the difficulty of interpreting probing assessments. When the probing pressure increased from 0.15N to 0.25N, BoP increased with 14% at implant sites. This increase was found to be significantly higher when compared to tooth sites (6.6%). A low probing force of 0.15N resulted in similar findings at implants and tooth sites. None of the selected papers gave detailed information on probing force. Only the paper by Chappuis et al. (2013) used the sulcus bleeding index instead of BoP. By doing so, there is no de-attachment of the mucosa around the implant as it is carried out without using a high force. This could explain the low bleeding score.

Merli et al. (2017) evaluated the peri-implant BoP together with PD scoring. They observed a 39% BoP and an increase in odds ratio by 1.8 for each 1 mm increment of PD. For pockets of 3 mm, 30%–40% were BoP-positive. Over 80% of the pockets of 7 mm were bleeding. Also, Farina et al. (2017) confirmed an odds ratio for BoP of 1.6 for each 1 mm increment of PD. In both studies, also similar proportion of BoP-positive sites was detected for pockets of 4 mm (27%) and 7 mm (60%). It is therefore obvious that deeper pockets have a higher tendency to bleed. A recent large retrospective cohort study (French et al., 2016) of nearly 5,000 Straumann implants placed in 2,060 patients with up to 10-year follow-up concluded that time alone and minimal bleeding did not correlate with bone loss but that care should be taken for implants with profuse bleeding or suppuration. They found the highest mean bone loss around implants with suppuration and minor changes for implants with minimal to moderate or profuse bleeding. They concluded that BoP around implants is a weak indicator of ongoing or future loss of crestal bone. The fact that BoP is a binary analysis of bleeding (bleeding or no bleeding) may possibly explain high false-positive bleeding scores. They suggested the use of an ordinal scale assessment to overcome this issue. In our review, only three of the 41 included papers used an ordinal scale, which may explain why the review could not find a significant correlation between reported prevalence and mean BoP and mean bone loss.

Suppuration is an unequivocal sign of inflammation that may be indicative of bone loss. In most clinical papers, suppuration as a diagnostic parameter is grouped together with bleeding and denoted as "BoP and/or suppuration." Only eight of 41 selected papers gave information about suppuration separately. Sanchez-Siles, Munoz-Camara, Salazar-Sanchez, Ballester-Ferrandis and Camacho-Alonso (2015) reported only two suppurating implants of the 120 implants diagnosed with peri-implantitis. On the other hand, in four other papers, the prevalence of suppurating implants strongly correlated with the reported prevalence. This latter finding is in accordance with the results of the study of French et al. (2016). They specified that suppuration was detected in implants with the highest bone loss and suggested it could be useful for clinical diagnosis. Confirmation in more studies seems essential to confirm this assumption.

5 | CONCLUSIONS

There is a large variation in the peri-implantitis case definitions, and reporting of biologic parameters is incomplete. Peri-implantitis prevalence did not correlate with diagnostic parameters mean PD, mean BoP, and mean bone loss. Only mean BoP correlated strong, with reported prevalence of peri-implantitis. Survival rate showed a substantial correlation with function time, with minor implant loss over time. Inconsistent reporting of peri-implantitis prevalence needs to be addressed, and an unambiguous case definition for peri-implantitis is of utmost importance for science as well as clinical practice.

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