# Peri-implantitis Risk Assessment (Pira)

# **Part 2: Retrospective Study and Framework**

# for an Evidence-Based Prediction Model for Clinicians

Running title:

Peri-implantitis risk assessment: online tool

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### Abstract

Aim: To develop an online tool based on an evidence-based predictive model, which allows clinicians to accurately predict the risk of peri-implantitis in candidates for dental implant therapy. Material & methods: A retrospective study of patients attending a university implant review clinic was performed. The presence of peri-implantitis and related risk factors were recorded. A predictive model for peri-implantitis was then developed based on this data. Results: 460 patients having 1,432 implants were included. Peri-implantitis was found in 78 (17%) patients. For partially edentulous patients (n=350, 60% female, average age 64.1

years), susceptibility to periodontitis (OR 0.48 [0.24;0.94], p = 0.03), the number of sites with probing pocket depth  $\ge 5$  mm (OR 0.2 [0.10;0.40], p < 0.01) and smoking (OR 0.25 [0.09;0.66], p < 0.01) were significantly associated with peri-implantitis. For fully edentulous patients (n=50, 72% female, average age 72.2 years), implants placed in the maxilla displayed a greater risk (OR 0.15 [0.02;0.87], p = 0.03) of developing periimplantitis. A predictive model for the development of peri-implantitis was created, based on 8 patient-related risk factors for partially edentulous patients (sensitivity = 90.2%, specificity = 55.0%) and 4 risk factors for fully edentulous patients (sensitivity = 100%, specificity = 51.3%). Conclusions: The predictive model can be used for a pre-operative risk assessment of partially edentulous patients. Further validation and refinement of the model with additional data could enable its use for fully edentulous patients, and will improve its predictive power, thereby increasing its reliability. *Int J Oral Maxillofac Implants* 2025;40:xxx-xxx. doi: 10.11607/jomi.11211

Key words: biofilm, bleeding on probing, bruxism, edentulism, general health, implant location, multi-causality, oral hygiene, periodontitis, peri-implantitis, prediction, predictive model, online tool, recall compliance, smoking, susceptibility to periodontitis, supportive periodontal therapy, teeth lost.

#### CLINICAL RELEVANCE

SCIENTIFIC RATIONALE FOR STUDY. This retrospective study investigated the effect of several risk factors on the development of peri-implantitis. It aimed to determine the relative importance of these factors and develop a model for the prediction of peri-implantitis.

PRINCIPAL FINDINGS. Susceptibility to periodontitis, the number of sites with deep ( $\geq 5$ 

mm) probing pocket depth and smoking were significantly associated with peri-implantitis in

partially edentulous patients. The predictive model successfully identified patients at

increased risk.

PRACTICAL IMPLICATIONS. Clinicians can use the predictive model when deciding if implant therapy is the best treatment option for their specific patient.

### Introduction

Peri-implantitis is a condition characterized by progressive bone loss around dental implants, ultimately leading to implant failure.<sup>1</sup> It affects around one in five dental implants.<sup>2</sup>

Oral diseases in general represent a global public health challenge, and peri-implantitis has a real potential of increasing this burden.<sup>3</sup> An increasing number of dental implants are placed every year, meaning prevention of the disease is crucial in reducing the impact of this disease in the future.<sup>4</sup> Early detection and management of peri-implant mucositis currently represents the primary prevention of the disease.<sup>5</sup>

A multitude of risk factors, some modifiable, are currently believed to be responsible for peri-implantitis. There is strong evidence that having a history of periodontitis, poor plaque control skills, no regular maintenance care after implant therapy increases the patient's risk of developing peri-implantitis (Schwarz et al., 2018) (see also Part 1 of this manuscript).

For other factors, such as smoking and diabetes, the latest consensus statement indicates that data are inconclusive. There is also limited evidence for an association with periimplantitis with factors such as post-restorative presence of submucosal cement, lack of periimplant keratinized mucosa, and improper positioning of implants which makes it difficult to maintain adequate oral hygiene 1. Moreover, several iatrogenic factors have been identified during the 7th European Workshop on Periodontology: "inadequate restoration-abutment seating, over-contouring of restorations, or implant malposition."<sup>6</sup>

Several models have been introduced to determine the risk of developing peri-implantitis either pre-operatively<sup>7,8</sup> or in already restored implants,<sup>9–11</sup> or to predict the progression of the disease once it is present.<sup>12–14</sup> The selection of risk factors and risk thresholds in many of these tools is based on expert opinion, which, while valuable, may introduce bias and limit their utility.

The aim of this project was to follow-up on the patient-related risk factors identified in the literature review in part 1, and assess their impact in a retrospective study of patients attending our implant review clinic. Based on this retrospective data, an evidence-based framework for constructing a "pre-operative" predictive model for peri-implantitis was created. This tool will be available online, and can be used by clinicians to assess their patients' risk for peri-implantitis at the treatment planning stage.

### **Materials & Methods**

### **Data Collection**

The records of patients attending our implant review clinic between December 2018 and December 2019 were examined, in order to estimate the impact of "patient-related" risk factors for peri-implantitis. Patients presenting with peri-implantitis and one of the following iatrogenic (treatment-related) risk factors were excluded: improper implant position, absence of keratinized attached mucosa around the implant, implant-level restorations using a non-biocompatible abutment material,<sup>15</sup> prosthetic restorations which made oral hygiene impossible (patient-reported), the presence of cement on intraoral radiographs. Additionally, records containing incomplete or missing data were also excluded. This study was approved by the Ethical committee of the University Hospital Leuven as study no. S65029.

### **Definitions**

We defined peri-implantitis as a radiographic distance from the implant platform to bone contact of  $\geq$  3 mm, in conjunction with bleeding on probing (BOP), as recommended for observational studies where initial radiographs may not always be available.<sup>16</sup> Moreover, the prevalence of peri-implantitis was reported at the patient-level, as recommended in the consensus report of the 8th European Workshop on Periodontology.<sup>17</sup>

An umbrella review performed in the first part of this project identified 10 patient-related risk factors reported in the medical literature. Because the risk factors which can be assessed differ greatly depending on the edentulism status of the patient, the patients in this study were divided into partially edentulous and fully edentulous subgroups. For partially edentulous patients, 8 risk factors were considered: susceptibility to periodontitis (bone loss / age), implant location, smoking, full mouth bleeding score, number of teeth lost, number of sites with PPD  $\geq$  5 mm, recall frequency, and general health (diabetes). Since data regarding various risk factors were not available for fully edentulous patients, only the following 4 risk factors were included for this group: implant location, smoking, recall frequency, and general health. Two potential risk factors identified in the literature were not assessed: oral hygiene (not available in file) and occlusal overload. Additionally, instead of history of periodontitis, which was identified in the literature, susceptibility to periodontitis 18, was used. The definitions of the risk factors and their diagnostic thresholds (respective categories used in the creation of the diagnostic tool) are summarized in Table 1.

			Partially	Fully
Risk factor	Description	Threshold	edentulous	edentulous
Susceptibility to	Alveolar bone loss as percentage /	≤ 0.5 / >	Х	
periodontitis1	patient age in years	0.5		
		$\leq 1 / > 1$		
Implant location	Lower / Upper arch		Х	X
Smoking1	Cigarettes smoked per day	0 / > 0	Х	Х
	Zero is used to indicate non-smoker			

 Table 1 Description of assessed risk factors and categories used in the univariate analysis.

		<pre>≤19/&gt;</pre>		
		19		
Full mouth bleeding	Percentage of sites displaying bleeding	<pre>&lt; 9 / &gt; 9</pre>	Х	
score1	on probing	<pre> ≤ 25 / &gt; </pre>		
		25		
Number of teeth lost1	Not including wisdom teeth	≤4/>4	Х	
		$\leq 8 / > 8$		
Number of periodontal		≤4/>4	Х	
pockets		$\leq 8 / > 8$		
with PPD $\geq 5 \text{ mm1}$				
Recall frequency	Number of months between recalls	$\leq 6 / > 6$	Х	Х
		≤ 12 / >		
		12		
General health	Diabetes		Х	Х

1 Threshold adopted from the periodontal risk assessment tool 18.

### Statistical Analysis

To validate the independence of the included risk factor variables, biplots were made based on a categorical principal component analysis. The arrows on the biplot unveil the relation between individual variables and the principal components. Principal components are a transformation of the data and are orthogonal variables, best summarizing the information in the data. The first component is the main component to describe the information held in the data set, the second component is a minor component. The vertical projection of the arrow end towards the component axes is called the loading for that variable with that component. The higher the loading of a variable with respect to a principal component, the higher the relation between that variable and the principal component. Hence, variables that have a high loading for the first principal component summarize the data the best.

Univariate relations were fit between peri-implantitis risk and each of the explanatory variables using a generalized linear model for binary data using a logit link. The values of continuous explanatory variables were divided into subgroups and odds ratios of differences between the groups were calculated using the regression coefficients of the generalized linear model. The relation between bone loss and peri-implantitis risk on the one hand and the explanatory variables was also assessed by a Spearman rank correlation coefficient. The relation with categorical variables was assessed with Cramer's V. Odds ratios were calculated for each variable, using thresholds previously defined in a periodontal risk assessment tool 18, but also using a receiver operating characteristic (ROC) analysis.

To construct a prediction model for peri-implantitis, a multivariable generalized linear model for binary data using a logit link was fit using the complete set of the explanatory variables. For fully edentulous patients, the explanatory variables were general health, implant location, smoking and time between recall appointments. For partially edentulous patients, this list was extended with susceptibility to periodontitis, full mouth bleeding score, number of sites with PPD >= 5 mm, and number of teeth lost. A receiver operating characteristic (ROC) analysis was fit between the predicted values from the generalized linear model and the peri-implantitis risk. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV), as well as likelihood ratios (LRs) were derived. LR+ describes the odds of developing peri-implantitis for a patient for which the model predicts peri-implantitis. It is the factor that the odds of the patient has for developing peri-implantitis before performing the test should be multiplied with, to obtain the post-test odds for not developing peri-implantitis. In addition, the importance/impact of each

variable was assessed by recalculating the generalized linear model with subsequent ROC analysis after leaving the variable out of the model.

#### **Online Tool**

An online tool implementing the predictive model has been developed (with the option to change the relative impact of each variable) and, once the accuracy of the predictive model is deemed high enough, will be available for free to clinicians.

#### Results

The records of 460 patients having 1,432 implants were examined. 78 patients had periimplantitis, resulting in a prevalence of 17%. The patients were split into two groups based on their dental status.

The partially edentulous group consisted of 391 patients, of which 41 were excluded because they presented with one or more iatrogenic factors. Of the remaining 350 patients, 210 (60%) were female, and the average age at examination was 64.1 years (range 23-90 years). The patients had 1,030 implants in total, with an average of 2.9 implants per patient. In this group, 46 patients (13.1%) had peri-implantitis.

The fully edentulous group consisted of 69 patients, of which 19 were excluded because they presented with one of more iatrogenic factors. Of the remaining 50 patients, 36 (72%) were female, and the average age at examination was 72.2 years (range 55-88 years). The patients had 162 implants in total, with an average of 3.2 implants per patient. In this group, 10 patients (20%) had peri-implantitis.

#### Principal Component Analysis

Figure 1 illustrates the results (loadings plots) of the principal component analysis for both groups by means of a biplot, on which only the loadings of the different variables are shown. For both partially and fully edentulous patients, no association could be found between the analyzed variables, with regard to their impact on the risk of developing of peri-implantitis.



**Fig 1** Loading plots of the principal component analysis for risk factors for partially edentulous (a) and fully edentulous patients (b). All variables have dissimilar loadings on both components, suggesting they are independent.

#### Univariate Analysis

For partially edentulous patients, susceptibility to periodontitis (bone loss/age) had a statistically significant odds ratio of 0.48 (95% CI [0.24;0.94], p = 0.03) when using the ROC analysis threshold (0.27), but not for the other defined thresholds. The number of sites with probing pocket depth (PPD)  $\geq$  5 mm produced statistically significant odds ratio for all analyzed thresholds (4, 8, and the ROC analysis result of 3), with 3 being the most pronounced with an OR of 0.2 (95% CI [0.10;0.40], p < 0.01). Non-smokers, when compared to smokers, had an odds ratio of 0.34 (95% CI [0.13;0.87], p = 0.03) for

developing peri-implantitis. There was insufficient data to calculate the odds ratio for heavy smokers (more than 19 cigarettes/day). The ROC analysis resulted in a threshold of 4 cigarettes/day, for which the odds ratio was 0.24 (95% CI [0.09;0.66], p < 0.01). The time between recalls, full mouth bleeding score, general health, implant location and the number of teeth lost did not result in statistically significant odds ratios.

For fully edentulous patients, implant location was the only variable with a statistically significant odds ratio of 0.15 (95% CI [0.02;0.87], p = 0.03) for implants placed in the lower vs. upper jaw. There was insufficient data to calculate the odds ratio for heavy smokers (more than 19 cigarettes/day), and a recall frequency of less than or equal to 6 months.

Further details regarding the odds ratios can be found in Table 2. The relation between the marginal bone level ( $\geq$  apical to the implant shoulder, or as a numerical value) and the above-mentioned variables (Spearman correlation, Cramer's V, and p-value) are available in Supplementary Table S1.

 Table 2 Odds ratios of univariate analysis of patient-related risk factors for peri-implantitis. Values which are associated with an increased risk of developing peri-implantitis are underlined.

Risk factor	Threshold	OR	p-value
Partially edentulous	1		
Susceptibility to periodontitis	≤ 0.5 / > 0.5	0.90 [0.45;1.78]	0.76
(bone loss / age)	$\leq 1 / > 1$	2.01 [0.24;15.90]	0.51
	≤ 0.27 / > 0.27a	0.48 [0.24;0.94]	0.03
Full mouth	≤ 9 / > 9	1.01 [0.54;1.89]	0.97
bleeding score	≤ 25 / > 25	0.73 [0.35;1.54]	0.41
(%)	≤ 12 / > 12a	0.79 [0.42;1.48]	0.47
General health problem	No / Yes	1.82 [0.92;3.61]	0.09
Implant location	Lower / Upper	1.59 [0.81;3.12]	0.18

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		0.01
$\leq 4 / > 4$	0.27 [0.14;0.52]	< 0.01
	0.26 [0.13;0.51]	< 0.01
≤ 3 / > 3a	0.2 [0.10;0.40]	0
≤ 4 / > 4	0.53 [0.27;1.05]	0.07
≤ 8 / > 8	0.66 [0.35;1.24]	0.20
$\leq 6 / > 6a$	0.61 [0.33;1.15]	0.13
0 /> 0	0.34 [0.13;0.87]	0.03
≤ 19 / > 19	Insufficient data	
≤4 />4a	0.25 [0.09;0.66]	< 0.01
≤ 6 / > 6	0.72 [0.16;3.25]	0.67
≤ 12 / > 12	0.68 [0.34;1.34]	0.26
≤13/>13a	0.80 [0.43;1.49]	0.48
No / Yes	1.26 [0.31;5.15]	0.74
Lower / Upper	0.15 [0.02;0.87]	0.03
0 /> 0	0.22 [0.02;1.96]	0.17
≤ 19 / > 19	Insufficient data	
≤1/>1a	0.22 [0.02;1.96]	0.17
Sime between recalls $\leq 6 / > 6$		I
≤ 12 / > 12	1.29 [0.30;5.59]	0.73
≤14/>14a	0.58 [0.14;2.38]	0.44
	$ \begin{array}{c c} \leq 3 / > 3a \\ \leq 4 / > 4 \\ \leq 8 / > 8 \\ \leq 6 / > 6a \\ 0 / > 0 \\ \leq 19 / > 19 \\ \leq 4 / > 4a \\ \leq 6 / > 6 \\ \leq 12 / > 12 \\ \leq 13 / > 13a \\ \end{array} $ No / Yes Lower / Upper 0 / > 0 \\ \leq 19 / > 19 \\ \leq 1 / > 1a \\ \leq 6 / > 6 \\ \leq 12 / > 12 \\ \end{array}	1 = 1 + 1 + 1 + 1 + 1 + 1 + 1 + 1 + 1 +

a Threshold determined using ROC analysis.

### **Predictive Models**

Because of incomplete or missing data, 29 patients and one patient were additionally excluded from the partially edentulous and fully edentulous groups, respectively. As a result, the predictive model included data from 321 partially edentulous and 49 fully edentulous patients.

For partially edentulous patients, PPV was 22.7%, NPV was 97.5%, with a sensitivity of 90.2% and specificity of 55% (and an LR+ of 2.0 and LR- of 0.2, respectively). When applying the model to the dataset, four of the 41 patients who had peri-implantitis, were predicted as having no risk. For fully edentulous patients, the positive and negative predictive values were 34.5% and 100%, respectively, with a sensitivity of 100%, and a specificity of 51.3% (and an LR+ of 2.0 and LR- of 0.0, respectively). No patients having peri-implantitis were predicted as having no risk.

These findings are further described in Table 3 (presenting the outcome of the predictive model when removing 1 of the included variables) and Supplementary Table S2. Supplementary Material 1 presents the equations used to calculate the risk for peri-implantitis for both partially and fully edentulous patients.

		Leaving out							
Variable Partially eden	Model	Susceptibility to	Full mouth bleeding score	General health	Implant location	# sites PPD $\ge 5 \text{ mm}$	# teeth lost	Smoking	Time between recalls
Faltially eden	luious								
PPV	22.7	26.4	24.7	21.3	24.4	28.2	26.6	25.8	26.0
NPV	97.5	94.3	97.7	96.2	94.8	92.8	96.4	95.4	95.5
Sensitivity	90.2	70.7	90.2	85.4	75.6	58.5	82.9	78.0	78.0
Specificity	55.0	71.1	59.6	53.9	65.7	78.2	66.4	67.1	67.5
LR+	2.01	2.45	2.24	1.85	2.21	2.69	2.47	2.38	2.40
LR-	0.18	0.41	0.16	0.27	0.37	0.53	0.26	0.33	0.33

Table 3 Accuracy and predictive values of the model.

Fully edentulous

PPV	34.5	50	44.4		33.3	35.7
NPV	100	89.2	85		100	100
Sensitivity	100	60	40		100	100
Specificity	51.3	84.6	87.2		48.7	53.8
LR+	2.05	3.9	3.12		1.95	2.17
LR-	0.0	0.47	0.69		0.0	0.0

PPV = positive predictive value, NPV = negative predictive value, LR = likelihood ratio.

### **Online Tool**

An online tool which implements the predictive model has been developed and will become available at the following address: https://pira.gbiomed.kuleuven.be. Because of the limited data for fully edentulous patients resulting in a less stable predictive model, it can currently only be used for a risk assessment of partially edentulous cases. Using this tool, the clinician can discuss with the patient which special precautions have to be taken, in order to reduce the potential risk for peri-implantitis development.

#### Discussion

The prevention of peri-implantitis is slowly becoming an integral part of implant therapy. It is a multi-factorial disease, and several of the identified risk factors are modifiable, providing both the clinician, through adequate treatment protocols, and the patient, through lifestyle changes, the opportunity to reduce the risk of developing the disease 1.

#### Existing Risk Assessment Tools

Several tools have been developed to predict the risk of developing peri-implantitis. The approach is not new, as it has been introduced two decades ago for periodontal risk

assessment.<sup>18,19</sup> The majority of the risk assessment tools for peri-implantitis are targeted at patients already having restored implants,<sup>10,11</sup> or even at patients presenting with peri-implantitis, with the aim to predict its progression and prognosis.<sup>12–14</sup> To the best of our knowledge, two tools currently target the pre-operative stage of treatment, assessing two<sup>20</sup> and three<sup>7</sup> risk factors, respectively.

A common limitation of many of these tools is that the risk factors taken into consideration are based on expert opinion. Furthermore, the thresholds for classifying individual factors as high-risk are also frequently chosen based on expert opinion. While interpreting the existing literature and using clinical experience for setting thresholds are of crucial importance when selecting the relevant risk factors, it may introduce biases and limit their utility. To mitigate this limitation, we used continuous variables wherever possible and also performed a ROC analysis to determine thresholds which best represent low- and highrisk categories.

Another important point is the potential of co-dependence of risk factors. Efforts should be made to identify independent risk factors which are simple to evaluate and provide a clear diagnostic threshold, reducing redundant measurements and avoidable errors. For instance, it is known that a history of periodontitis is a significant predictor for compliance with recall appointments, while smokers are associated with lower compliance.<sup>21</sup> Our principal component analysis was an attempt to identify potential associations between the assessed risk factors. The fact that no interactions were found for the chosen variables, justified their use in the model.

## **Risk Factor Selection**

The selection of the patient-related risk factors was supported by an umbrella review of systematic reviews and/or meta-analyses (see part 1). Based on the results of this extensive search, 10 relevant patient-related risk factors were identified.

The risk factors in the predictive model are mostly compatible with the consensus conference recommendations 1. They are listed, along with risk factors assessed by other risk assessment tools, in Supplementary Table S3. We decided to make some slight adjustments, however, which we explain below. First, instead of history of periodontitis, we analyzed susceptibility to periodontitis, defined as the ratio between the percentage of alveolar bone loss and patient age.<sup>18</sup> The reason behind this decision was that susceptibility is a continuous variable and removes any subjectivity introduced by a pre-defined threshold. Secondly, we did not consider oral hygiene levels and plaque scores, because of the inconsistent measurement methodology in our records (assessment was performed by multiple uncalibrated clinicians, with and without plaque disclosure, and several plaque scores were used). Finally, we decided to not assess bruxism and occlusal overload, because of the relatively subjective diagnostic criteria used.

When looking at the deep periodontal pockets as a sign of active periodontal disease, multiple thresholds have been considered. One tool considers the number of pockets with  $PPD \ge 5 \text{ mm}$ ,<sup>10</sup> while another considers the percentage of pockets with  $PPD \ge 6 \text{ mm}$ .<sup>8</sup> It is possible that assessing a continuous variable and its relation to bone loss would give a clearer picture, but this would require a full periodontal chart to be recorded at each recall appointment. We therefore chose the number of pockets having a probing depth of 5 mm or more as our threshold.

Recall appointments, compliance, and plaque control are used interchangeably as risk factors 1. Further, the thresholds for these variables are heterogeneous. While it is clear that

they are related, and that biofilm is a requirement for the development of the disease, this has resulted in researchers investigating several different aspects (recall interval, compliance, various plaque scores), making comparisons difficult. We used the average interval between recall appointments in the last 10 years or since loading, whichever was shorter.

Another innovative approach was the use of iatrogenic risk factors to exclude patients whose peri-implantitis could be 'explained'. While the selection of iatrogenic risk factors and their thresholds is certainly debatable, we believe it did allow us to improve the data by removing peri-implantitis cases for which the explanation was treatment- rather than patientrelated.

### **Findings**

In the case of partially edentulous patients, susceptibility for periodontitis reached a significant threshold when setting the threshold using the ROC analysis, but did not reach statistical significance for the other pre-defined thresholds. The number of periodontal pockets with PPD  $\geq$  5 mm was significant for all chosen thresholds, suggesting that active periodontal disease may play a stronger role in the development of peri-implantitis. There was insufficient data to determine the odds ratio for heavy smokers ( $\geq$  20 cigarettes / day).

The sample size of the fully edentulous group was small (n=50), and as a result there was insufficient data to determine the odds ratio for heavy smokers and a recall threshold of 6 months. Interestingly, patients in this group presented more risk when their implants were placed in the maxilla. The predictive model for this group also proved unstable, and as a result we were not able to include it in the predictive tool at this stage.

# **Clinical Applications**

The online tool, which is based on our predictive model, can be used by clinicians considering implant therapy in two ways: first, to calculate the risk for a specific patient and determine whether they are a good candidate for implant therapy; second, by discussing the risk factors with the patient and focusing on the modifiable risk factors (that the patient can change in order to reduce their risk of developing peri-implantitis), thereby providing concrete, actionable advice and actively involving the patient in the treatment.

### Limitations

Even though every effort was made to ensure the high quality of the data and of the resulting model, this study does suffer from several limitations. First, it is a retrospective study, meaning it can at best only infer associations of risk indicators with the disease, and cannot be used to identify causal risk factors.<sup>22</sup> Further, the study was performed in a single university clinic using a convenience sample of patients attending recall appointments.

While this review was performed using a systematic methodology, it assessed risk factors identified in systematic reviews only, meaning that it did not consider all risk factors mentioned in the literature. There is, of course, also the possibility that some risk factors are yet unknown to our field.

Regarding the assessed risk factors, oral hygiene and occlusal overload were not included because of the reasons given previously, even though these have been identified as potential risk factors in the umbrella review.

Ten percent of the partially edentulous patients and a surprising twenty eight percent of the fully edentulous patients were excluded because one or more iatrogenic factors were present. This may be due to the fact that many of the patients in this study were treated by postgraduate students who are still climbing the learning curve, and also because of changes in treatment approaches over time (e.g. the importance given to keratinized tissue today compared to 15-20 years ago).

Furthermore, the predictive model based on the available data considers recall interval to be a (slightly) protective factor for peri-implantitis, implying that patients who attend the clinic more frequently are more likely to develop the disease. After considering potential causes for this unexpected finding, which goes against the existing literature and guidelines, we hypothesized that this is a limitation of the retrospective nature of the study, as patients with peri-implantitis may attend more frequently for treatment of the disease, rather than for a regular recall. To overcome this limitation, we have corrected for recall frequency manually, considering it a risk factor for developing peri-implantitis.

Finally, the available data for fully edentulous patients was limited, resulting in an unstable model which is not yet ready for clinical use. Both models are slightly overly cautious, potentially predicting risk of disease where there may be none.

Nevertheless, we believe this paper introduces a novel approach on which to build an evidence-based predictive model for the pre-operative assessment of patient-level periimplantitis risk. The model can provide valuable information for partially edentulous patients and has been made freely available to clinicians. The inclusion of more patients (and more centers) would further improve the existing model, which is easily adaptable. The current results formed the basis for a prospective multicenter trial, which is in planning and should further increase both the quality and quantity of available data, and hopefully also expand the model's applicability to fully edentulous patients.

#### Conclusions

The prevention of peri-implantitis must play a pivotal role in implant therapy. This paper introduces an evidence-based framework for the development of a predictive model for preoperative peri-implantitis risk assessment, which has the potential to allow clinicians to detect candidate patients for implant therapy that are at high risk for developing peri-implantitis, and discuss modifiable risk factors with patients, which can be influenced for example through lifestyle choices, potentially lowering their risk for developing the disease. Additional data are required to improve the model and a prospective multicenter trial most likely represents the best approach to obtain it.

#### **Supplemental Materials and Tables**

Supplemental materials will be available in the final version of this article.

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Conflict of interest:

All (co)-authors declare that they have no conflict of interest. The department of periodontology owns research chairs from several implant companies: Dentsply Sirona, Straumann, Henry Schein. This study was partially supported by a grant from Nobel Biocare and Dentsply Sirona.

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