

Validation of a multivariate prediction rule for history of periodontitis in a separate population

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Abstract

Aim: Validation of a previously derived prediction rule for periodontitis in an external population sample.

Materials and Methods: Age, smoking and self-reported tooth mobility were used in logistic models to predict moderate and severe periodontitis as diagnosed from panoramic radiographs of 246 patients attending private practices in Germany. Coefficients derived from these models were used to predict periodontitis in a representative population-based sample of 3297 residents of the region of Pomerania, Germany.

Results: In the full derivation sample, the predictive power of the logistic model as measured by the *c*-statistic was 0.82 and 0.84 for moderate and severe periodontitis, respectively. In the validation set, these models yielded *c*-statistics of 0.82 for both moderate and severe periodontitis. Lower *c*-statistics were obtained among subjects aged 40 years and older in the derivation set (*c* = 0.74 and 0.77), and the performance was poorer in the validation set with *c*-statistics of 0.69 and 0.72, respectively.

Conclusions: A prediction rule based on age, smoking and self-reported tooth mobility can yield a moderately useful external validity. Validity may be dependent on specific population characteristics, and derivation of a prediction rule based on a clinical subsample of the target population with a larger set of predictors may provide better results in an application.

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Periodontitis is a common chronic inflammatory disease that is a major cause of tooth loss and may also be a risk factor for various systemic conditions and diseases. Large epidemiologic studies are needed to identify determinants of periodontitis risk as well as consequences of periodontitis in various populations. However, the diagnosis of periodontal disease is typically based on a thorough clinical and radiographic examination, which limits the feasibility to assess periodontal disease as an exposure or an outcome in large epidemiologic studies. Self-reported periodontal measures could provide a highly cost-efficient means of ascertaining perio-

dontal disease in such studies. Indeed, self-reported periodontitis has been validated and applied in large cohort studies of health professionals (Joshipura et al. 1996a, b, 2002, 2003). Studies in populations other than health professionals have shown mixed results (Blicher et al. 2005), and any single individual question (including simple combinations of related questions) was unable to assess periodontal disease with satisfactory accuracy in a general population (Dietrich et al. 2005).

More recently, several groups have evaluated the performance of multivariate prediction rules that combine information from self-reported periodontitis

or periodontitis symptoms and established risk factors for periodontitis in logistic regression models to ascertain periodontitis (Dietrich et al. 2007, Gilbert & Litaker 2007, Slade 2007, Taylor & Borgnakke 2007). Of the many different self-reported periodontal items that were evaluated in these studies, self-reported tooth mobility was consistently found to be a highly significant predictor of both moderate and severe periodontitis using various different periodontal disease definitions (Dietrich et al. 2007, Gilbert & Litaker 2007, Slade 2007, Taylor & Borgnakke 2007). Self-reported tooth mobility by itself has a relatively low sensitivity but has consistently been shown to have a specificity of more than 90% for the diagnosis of moderate or severe periodontitis (Dietrich et al. 2007, Gilbert & Litaker 2007, Taylor & Borgnakke 2007). The multiple logistic regression models developed to predict periodontal disease based on self-reported items and established risk factors typically yielded *c*-statistics in the range of 0.7–0.8, indicating that such a prediction rule could potentially be useful for surveillance and epidemiologic research (Swets 1988).

However, none of these models has been validated in a different population, which is important because a prediction rule derived from one sample does not necessarily perform well in a different sample or population.

The purpose of the present study was therefore to derive a prediction rule for moderate and severe periodontal disease based on self-reported tooth mobility and established periodontal risk factors in a German practice-based sample (Dietrich et al. 2005, 2007), and to validate this prediction rule in a large representative German population sample.

Study Design and Setting

Study subjects

Derivation sample

The derivation sample was a practice-based convenience sample of patients referred for endodontic surgery by general dentists to one of two private practices for Oral and Maxillofacial Surgery in Germany and has been described previously (Dietrich et al. 2005, 2007). Briefly, patients who were 20- to 80-year-old German speakers, had at least 10 remaining teeth and had a recent panoramic radiograph for assess-

ment of alveolar bone loss (ABL) available were enrolled in 2002–2003. The study protocol was approved by the Institutional Review Board of the Charité Medical School in Berlin. Patients completed a self-administered questionnaire including a question on tooth mobility ('Have you ever noticed the loosening of a single tooth?'). The questionnaire also ascertained cigarette smoking history as never (<100 lifetime cigarettes), former or current smoking.

For the assessment of the gold standard diagnosis (positive history of periodontal disease), panoramic radiographs were read by a single dentist who was blinded to the subjects' responses to the questionnaire (Dietrich et al. 2005). For the present analyses, we used two periodontal disease definitions based on the CDC working group definitions (Page & Eke 2007), but modified for ABL measures as assessed on panoramic radiographs (Pilgram et al. 2000, Persson et al. 2003, Dietrich et al. 2007). Accordingly, moderate periodontitis was defined as ≥ 2 teeth with ABL ≥ 5 mm and severe periodontitis was defined as ≥ 2 teeth with ABL ≥ 7 mm.

Validation sample

The Study of Health in Pomerania (SHIP) is a population-based representative cross-sectional survey involving three cities and 29 surrounding towns and villages in the north-east of Germany. First, the three cities and 12 towns of the region with >1500 inhabitants were selected, and then 17 of 97 smaller towns and villages (<1500 inhabitants) were selected randomly. Second, from each of these, German subjects with main residency in the area were drawn at random, proportional to each community population size and stratified by age and gender. Thus, a representative sample of 7008 adults aged 20–79 years was invited to participate. This two-stage cluster sampling method yielded twelve 5-year age strata (20–79 years) for both sexes. After excluding 746 individuals who had died, moved away or had severe medical problems, 6262 inhabitants were invited to participate. The final observed sample included 4310 individuals, yielding an overall participation rate of 68.8%. Details regarding the design, recruitment and scope of the oral health component of SHIP have been published previously (Hensel et al. 2003). All participants gave writ-

ten informed consent, and the study was approved by the local ethics committee.

The oral examination was performed by trained and calibrated dental examiners. SHIP utilized a partial-mouth periodontal assessment of all fully erupted teeth alternately in the left or the right half of the mouth, with third molars excluded. Attachment loss and probing depth were assessed at four sites (mesiobuccal, distobuccal, midbuccal and midlingual) per tooth with a periodontal probe (PCP 11, HuFriedy, Chicago, IL, USA) to the nearest millimetre. For the present analysis, we defined subjects with at least two teeth with inter-proximal (mesiobuccal or distobuccal) clinical attachment loss (CAL) of ≥ 4 and ≥ 6 mm as having a history of moderate and severe periodontitis, respectively. As the focus of this analysis is on a history of periodontitis and to be consistent with the radiographic assessments made in the derivation sample, probing depth was not a criterion for the definition of periodontitis (Page & Eke 2007). Self-reported tooth mobility was assessed by a dichotomous question ('Do you have loose teeth?').

In addition, participants were classified as never, former or current cigarette smokers based on their interview responses.

Statistical analyses

For the derivation sample, detailed analyses regarding the bivariate association of item responses and radiographic diagnosis of periodontitis (Dietrich et al. 2005), as well as the derivation of a multivariate prediction rule based on a logistic regression model have been described previously (Dietrich et al. 2007). Briefly, self-reported tooth mobility was invariably selected for predictive models using various variable selection methods and periodontal disease definitions, together with age and smoking. One or two additional self-reported items were included in these predictive models (Dietrich et al. 2007). However, because we had no data on any of these additional items in the validation sample (SHIP), completely pre-specified logistic regression models were fit in the derivation sample using age and smoking (never, former, and current) and self-reported tooth mobility as independent variables. Separate models were fit for moderate and severe periodontitis definitions. The *c*-statistic

Table 1. Characteristics of the derivation sample and validation sample by periodontal status

	Derivation sample				Validation sample			
	2+teeth 5+ mm ABL		2+teeth 7+ mm ABL		2+teeth 4+ mm CAL		2+teeth 6+ mm CAL	
	no <i>n</i> = 124 (50%)	yes <i>n</i> = 122 (50%)	no <i>n</i> = 208 (85%)	yes <i>n</i> = 38 (15%)	no <i>n</i> = 1464 (44%)	yes <i>n</i> = 1833 (56%)	no <i>n</i> = 2467 (75%)	yes <i>n</i> = 830 (25%)
Age (years), mean (SD)	36 (10)	48 (13)	40 (12)	52 (13)	38 (13)	53 (13)	43 (14)	56 (12)
Female no. (%)	71 (57)	73 (60)	126 (60)	18 (47)	841 (57)	842 (46)	1369 (55)	314 (38)
Smoking no. (%)								
Never	52 (42)	34 (28)	76 (36)	10 (26)	537 (37)	640 (35)	920 (37)	257 (31)
Former	28 (23)	47 (38)	61 (29)	14 (37)	431 (29)	651 (36)	767 (31)	315 (38)
Current	44 (35)	41 (34)	71 (34)	14 (37)	496 (34)	542 (30)	780 (32)	258 (31)
Alveolar bone loss (mm) mean (SD)	2.5 (0.4)	3.9 (1.0)	2.9 (0.6)	4.8 (1.0)	—	—	—	—
Attachment loss (mm) mean (SD)	—	—	—	—	2.0 (0.6)	4.1 (1.5)	2.4 (0.9)	5.1 (1.5)
Self-reported tooth mobility no. (%)	9 (7)	31 (25)	23 (11)	17 (45)	55 (4)	352 (19)	155 (6)	252 (30)

ABL, alveolar bone loss; CAL, clinical attachment loss; SD, standard deviation.

(area under the ROC curve) and two-sided 95% confidence intervals (CI) were calculated as a measure of the discriminatory performance of the prediction rule. Separate models were also fit for a sample restricted to subjects aged 40 years and older. The β coefficients of these models were then used to calculate predicted probabilities of periodontitis in the validation sample (SHIP). For comparison purposes, we also fit separate logistic regression models in the SHIP dataset. Again, the *c*-statistic was calculated as a measure of discriminatory ability. Swets (1988) has defined *c*-statistics of 0.7–0.9 as ‘useful’. In addition, sensitivity and specificity with exact 95% confidence intervals were calculated for self-reported mobility as well as for the prediction rule in the validation sample. For the latter, the sample-predicted probability was used as a cut-off to define moderate or severe periodontitis that yielded the observed prevalence in the derivation set (Dietrich et al. 2007), as proposed by Slade (2007). Because estimation of periodontitis prevalence may be another important application of a prediction rule (Eke & Genco 2007), we derived estimates for prevalences of moderate and severe periodontitis based on predicted probabilities in the validation set (LaVange & Koch 2007) and compared it with the observed prevalences.

Two-sided 95% confidence intervals were calculated as appropriate using a statistical package (STATA 7.0, Stata Corp., College Station, TX, USA).

Results

The derivation sample consisted of 246 subjects with a mean age of 40 years (range: 20–80 years), as described previously (Dietrich et al. 2005) (Table 1). In the validation sample (SHIP), a total of 3332 subjects had inter-proximal periodontal assessments on at least two teeth. After exclusion of 35 subjects with missing data on self-reported tooth mobility or smoking history, the final sample consisted of 3297 individuals with a mean age of 46 years (range: 20–81 years, Table 1).

In the derivation sample, the proportion of patients with moderate/severe and severe periodontitis was 50% and 15%, respectively, compared with 56% and 25% in the validation sample.

Self-reported tooth mobility had 25% (95% CI: 18%, 34%) sensitivity and 93% (87%, 97%) specificity for moderate periodontitis, and 45% (29%, 62%) sensitivity and 89% (84%, 93%) specificity for severe periodontitis in the derivation sample. In the validation set, the sensitivity was 19% (17%, 21%) and the specificity was 96% (95%, 97%) for moderate periodontitis. For severe periodontitis, the sensitivity was 30% (27%, 34%) and the specificity was 94% (93%, 95%).

The β coefficients and associated *p*-values for the logistic models fit in the derivation set are shown in Table 2. Self-reported tooth mobility was a significant independent predictor of both moderate and severe periodontitis. In the full derivation sample, the predictive

power of the logistic model as measured by the *c*-statistic (area under the ROC curve) was 0.82 and 0.84 for moderate and severe periodontitis, respectively (Table 3). The application of this prediction rule in the validation set yielded very similar *c*-statistics of 0.82 for both moderate and severe periodontitis definitions. The best-fitting model using the same set of predictors in the validation set did not result in improved discriminatory power (*c* = 0.82 for both moderate and severe periodontitis, Table 3). The discriminatory power of the logistic model fit separately among subjects in the derivation set aged 40 years and older was *c* = 0.74 and 0.77 for moderate and severe periodontitis, respectively. The performance of this prediction rule was lower in the validation set with *c*-statistics of 0.69 and 0.72, respectively (Table 3). The best-fitting model using this set of predictors in the validation set yielded *c*-statistics of 0.70 and 0.73, respectively. Unlike in the derivation set, gender was a significant independent predictor of periodontitis in the validation set. Adding gender to the set of predictors in the models fitted in the validation set increased the *c*-statistics of all models by one percentage point (data not shown). The sensitivities and specificities of the logistic models when predicted probabilities were dichotomized to yield observed prevalences of moderate and severe periodontitis are reported in Table 3.

The estimates of moderate and severe periodontitis in the entire validation

Table 2. β coefficients and p -values for logistic models fit in the derivation sample (separate models for full sample and sample restricted to subjects 40+ years old and separate models for moderate and severe periodontitis definitions)

	Full sample (20–80 years)						Subjects aged 40+ years					
	2+teeth 5+ mm ABL			2+teeth 7+ mm ABL			2+teeth 5+ mm ABL			2+teeth 7+ mm ABL		
	n^*	β	p -value	n^*	β	p -value	n^*	β	p -value	n^*	β	p -value
Age (years)	122	0.10	<0.001	38	0.09	<0.001	89	0.08	0.003	31	0.073	0.01
Smoking (reference: never)												
Former	47	0.98	0.012	14	0.71	0.176	40	1.14	0.023	13	0.51	0.357
Current	41	1.09	0.006	14	1.28	0.038	22	1.37	0.034	8	0.66	0.364
Self-reported tooth mobility	31	1.54	0.001	17	1.85	<0.001	23	1.20	0.082	14	1.84	0.001
Constant		–5.05	<0.001		–6.93	<0.001		–4.33	0.005		–5.91	0.001

* n , number of patients with periodontitis.

ABL, alveolar bone loss.

Table 3. C -statistics for logistic models and sensitivities and specificities (for cut-off based on observed prevalence) for moderate and severe periodontitis definitions (95% confidence intervals in parentheses)

	Full sample (20–80 years)			Subjects aged 40+ years		
	Derivation set ($n = 246$)	Validation set* ($n = 3297$)	Validation set† ($n = 3297$)	Derivation set ($n = 124$)	Validation set* ($n = 2089$)	Validation set† ($n = 2089$)
2+teeth 5+ mm ABL						
C -statistic	0.82 (0.77, 0.87)	0.82 (0.81, 0.83)	0.82 (0.81, 0.84)	0.74 (0.66, 0.82)	0.69 (0.67, 0.69)	0.70 (0.68, 0.72)
Sensitivity	74% (65%, 81%)	78% (76%, 80%)	78% (76%, 80%)	82% (72%, 89%)	80% (78%, 82%)	80% (78%, 82%)
Specificity	75% (66%, 82%)	72% (70%, 74%)	73% (70%, 75%)	57% (39%, 74%)	44% (40%, 48%)	45% (41%, 49%)
2+teeth 7+ mm ABL						
C -statistic	0.84 (0.79, 0.88)	0.82 (0.80, 0.83)	0.82 (0.81, 0.83)	0.77 (0.69, 0.84)	0.72 (0.70, 0.74)	0.73 (0.71, 0.75)
Sensitivity	45% (29%, 62%)	55% (51%, 58%)	55% (51%, 58%)	48% (30%, 67%)	57% (53%, 60%)	57% (54%, 61%)
Specificity	91% (87%, 95%)	85% (84%, 87%)	85% (84%, 87%)	83% (74%, 90%)	75% (72%, 77%)	75% (72%, 77%)

*Model with β coefficients derived from the derivation set.†Model with β coefficients derived from the validation set.

Separate models for full sample and sample restricted to subjects 40+ years old and separate models for moderate and severe periodontitis definitions.

sample based on the prediction rule were 57% (compared with 56% observed) and 21% (observed: 25%), respectively. For the subsample of subjects aged 40 years and older, the estimates of moderate and severe periodontitis prevalence were 74% (observed: 74%) and 27% (observed: 37%).

Discussion

Single self-reported items may not be able to accurately assess periodontal disease history in general populations (Blicher et al. 2005). Recent studies have therefore attempted to use self-reported items and basic demographic and behavioural variables that constitute established periodontal risk factors in logistic regression models to assess periodontitis (Dietrich et al. 2007, Gen-

co et al. 2007, Gilbert & Litaker 2007, Slade 2007, Taylor & Borgnakke 2007). The results of the present study suggest that a simple prediction rule based on age, smoking and self-reported tooth mobility may yield useful discrimination between subjects with and without a history of periodontitis, and that such a prediction rule provides useful accuracy in a different population.

Of the many self-reported items that have been evaluated to assess periodontitis, self-reported mobility has consistently been found to be a strong predictor of periodontitis (Blicher et al. 2005, Dietrich et al. 2005, Gilbert & Litaker 2007, Taylor & Borgnakke 2007). Furthermore, it was consistently found to be an independent predictor in multivariate prediction rules (Dietrich et al. 2007, Gilbert & Litaker 2007, Slade 2007, Taylor & Borgnakke 2007). Con-

firmed previous results (Dietrich et al. 2005, Gilbert & Litaker 2007, Taylor & Borgnakke 2007), the present study found self-reported tooth mobility to have high specificity, but low sensitivity. This makes intuitive sense as tooth mobility is a relatively late symptom of periodontal bone loss and other causes of tooth mobility are relatively rare when compared with periodontitis. More recent cognitive testing of questions for periodontitis-related tooth mobility indicated that the question should specifically exclude deciduous teeth and tooth mobility due to trauma (Miller et al. 2007). However, neither the question in the derivation nor the validation sample made these exclusions. Hence, the specificity of self-reported tooth mobility may be even higher than reported here.

Consistent with our previous findings in the derivation sample (Dietrich et al.

2007), we found that the prediction rule performed better when applied to the full sample including the entire age range than in a subset of subjects aged 40 years and older. This also held in the validation set and can be attributed to the dominant effect of age on the prediction of periodontitis history in a sample with a wider age range (Dietrich et al. 2007). Furthermore, in contrast to the full sample, the predictive power of the prediction rule was also notably smaller in the validation set than in the derivation set among subjects 40 years or older. However, fitting a logistic model in the validation set using the same set of predictors increased the *c*-statistic by only one percentage point, and adding gender to the model increased the *c*-statistic by just another percentage point. Hence, the weights (β -coefficients) derived from the derivation set performed reasonably well in the validation set, while these predictors had a somewhat lower validity in the validation set compared with the derivation set. Further analyses revealed that smoking was a stronger predictor of periodontitis history in the derivation set than in the validation set as measured by the *c*-statistic (results not shown). The differences in the *c*-statistics between the full sample and the subgroup aged 40 years and older also translated into differences in the accuracy of the predicted prevalences of moderate and severe periodontitis.

The sensitivities and specificities shown in Table 3 are based on dichotomizing the predicted probabilities of the prediction rule and are shown for illustrative purposes. In an application, an investigator may choose different cutoffs to yield a higher specificity at the expense of a lower sensitivity, or vice versa (Dietrich et al. 2007).

In conclusion, the results of the present study show that a prediction rule based on age, smoking and self-reported tooth mobility derived from a practice-based sample can yield a moderately useful accuracy in a population-based study with a wide age range. However, the accuracy may be lower in specific

subgroups. Furthermore, the validity of a prediction rule may be dependent on specific population characteristics and derivation of a prediction rule based on a clinical sub-sample of the target population, including a larger set of predictors, may provide better results.

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Clinical Relevance

Scientific rationale for the study: Information on self-reported tooth mobility and established periodontal risk factors may be useful as a surrogate measure of periodontitis in epidemiologic applications.

Principal findings: A prediction rule for periodontitis based on age, smoking and self-reported tooth mobility derived from a practice-based sample was moderately useful to predict periodontitis in a population-based representative sample.

Practical implications: A simple, previously derived prediction rule may be useful in epidemiologic applications. However, derivation of a prediction rule based on a sub-sample of the target population may provide better results.

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