

# Prediction of periodontal disease: modelling and validation in different general German populations

Yiqiang Zhan<sup>1</sup>, Birte Holtfreter<sup>1</sup>, Peter Meisel<sup>1</sup>, Thomas Hoffmann<sup>2</sup>, Wolfgang Micheelis<sup>3</sup>, Thomas Dietrich<sup>4</sup> and Thomas Kocher<sup>1</sup>

<sup>1</sup>Unit of Periodontology, University Medicine, Ernst-Moritz-Arndt University Greifswald, Greifswald, Germany; <sup>2</sup>Department of Periodontology, Medical Faculty Carl Gustav Carus, Dresden, Germany; <sup>3</sup>Institute of German Dentists, Köln, Germany; <sup>4</sup>Department of Oral Surgery, School of Dentistry, University of Birmingham, Birmingham, UK

Zhan Y, Holtfreter B, Meisel P, Hoffmann T, Micheelis W, Dietrich T, Kocher T. Prediction of periodontal disease: modelling and validation in different general German populations. *J Clin Periodontol* 2014; 41: 224–231. doi: 10.1111/jcpe.12208.

## Abstract

**Aim:** To develop models for periodontitis using self-reported questions and to validate them externally.

**Methods:** The Study of Health in Pomerania (SHIP-0) was used for model development. Periodontitis was defined according to the definitions of the Center for Disease Control and Prevention-American Academy of Periodontology, the 5th European Workshop in Periodontology, and Dietrich et al. ( $\geq 2$  teeth with inter-proximal clinical attachment loss of  $\geq 4$  mm and 6 mm as moderate and severe periodontitis) respectively. These models were validated in SHIP-Trend and the Fourth German Oral Health Study (DMS IV).

**Results:** Final models included age, gender, education, smoking, bleeding on brushing and self-reported presence of mobile teeth. Concordance-statistics (C-statistics) of the final models from SHIP-0 were 0.84, 0.82 and 0.85 for the three definitions respectively. Validation in SHIP-Trend revealed C-statistics of 0.82, 0.81 and 0.82 respectively. As bleeding on brushing and presence of mobile teeth were unavailable in DMS IV, reduced models were developed. C-statistics of reduced models were 0.82, 0.81 and 0.83 respectively. Validation in DMS IV revealed C-statistics of 0.72, 0.78 and 0.72 for the three definitions respectively. All *p* values of the goodness-of-fit tests were  $>0.05$ .

**Conclusions:** The models yielded a moderate usefulness for prediction of periodontitis.

Key words: external validation; periodontitis; self-reported measures; Study of Health in Pomerania (SHIP); the Fourth German Oral Health Study (DMS IV)

Accepted for publication 28 November 2013

Periodontitis is a common chronic inflammatory disease, which may be related to various systemic diseases, such as diabetes (Lalla & Papapanou 2011, Engebretson & Kocher 2013), coronary heart disease (Dietrich et al. 2013) and pre-term delivery or low birth weight (Chambrone et al. 2011, Ide & Papapanou 2013). Thus,

## Conflict of interest and source of funding statement

The authors declare that they have no conflict of interests.

SHIP is part of the Community Medicine Research net (<http://www.mezizin.uni-greifswald.de/cm>) of the University of Greifswald, Germany, which is funded by the German Federal Ministry of Education and Research (BMBF, grant 01ZZ96030, 01ZZ0701), the Ministry of Education, Research and Cultural Affairs as well as the Ministry of Social Affairs of the Federal State of Mecklenburg-West Pomerania. Y.Z. was supported by RAPID (Rheumatoid Arthritis and Periodontal Inflammatory Disease, grant number 290246), 7th framework programme of the EU. B.H. was supported by an unlimited educational grant from GABA, Switzerland. Further support was provided by the Deutsche Gesellschaft für Parodontologie (DGParo) e.V.

the prevalence of periodontitis has been of increasing concern around the world for the last decades. In the US, around 30.0% and 8.5% of adults had moderate or severe periodontitis in 2009 and 2010 (Eke et al. 2012). According to the Fourth German Oral Health Study (DMS IV) conducted in 2005 (Holtfreter et al. 2010), the prevalence of clinical attachment loss (CAL)  $\geq 3$  mm was 95.0% in adults and 99.2% in seniors, while that of probing depth (PD)  $\geq 4$  mm was 76.9% and 87.7% in adults and seniors respectively. Periodontitis is a serious public health problem in the western world, and there is an urgent need for surveillance, to investigate the aetiology of periodontitis, to study the secular trends and to develop preventive and treatment strategies.

To assess the prevalence of periodontitis, thorough clinical and radiographic examinations are the typical tools for most of the present epidemiological studies. However, these methods are usually expensive, resource-demanding and time-consuming. Consequently, alternative cost-effective but reliable and valid instruments for periodontitis prevalence surveillance at the national or state level, such as scales or questionnaires, are on the agenda of the scientific community. The Center for Disease Control and Prevention (CDC) and the American Academy of Periodontology (AAP) proposed some questions to assess periodontitis (Page & Eke 2007), which were later used in the CDC Periodontal Disease Surveillance Project (Eke & Genco 2007, Eke et al. 2013). Dietrich and colleagues also developed a model to assess periodontitis, which had a moderate prediction performance for different German clinical samples (Dietrich et al. 2005, 2007, 2009). In addition, some other research groups developed prediction models using self-reported measures to study periodontitis (Joshi et al. 1996, Blicher et al. 2005, Eke & Genco 2007, Gilbert & Litaker 2007). However, few of these studies validated their prediction models in a different population. Thus, it is reasonable to develop models for periodontitis from community-based populations, and to externally validate them in other similar community-based populations.

The purposes of present study were: (i) to develop prediction models for current population prevalence of periodontitis using a combination of self-reported questions and demographic characteristics from the Study of Health in Pomerania (SHIP-0) with different definitions of periodontitis; (ii) to externally validate these models in the cohorts of SHIP-Trend and DMS IV.

## Material and Methods

### Study samples

#### SHIP-0

SHIP-0 is a cross-sectional survey using a two-stage cluster sampling design conducted between 1997 and 2001. The details about the study design were reported elsewhere (Volzke et al. 2011). In brief, 7008 inhabitants were sampled from the source population. Due to death, emigration or medical problems with respect to periodontal probing (haemophilia and risk of endocarditis), 746 subjects were excluded. For the rest of 6262 subjects, the response rate was 68.8% (Hensel et al. 2003), resulting in 4308 participants.

#### SHIP-Trend

SHIP-Trend is a cohort in the same area as SHIP-0. Baseline examinations were conducted between 2008 and 2012. A stratified random sample of 8016 adults aged 20–79 years was drawn from population registries. Sample selection was facilitated by centralization of local population registries in the Federal State of Mecklenburg/West Pomerania. Stratification variables were age, sex and city/county of residence. The target sample size was chosen to obtain a final sample size similar to that of SHIP-0. Finally, 4248 subjects participated in the survey.

#### DMS IV

The Fourth German Oral Health Survey (DMS IV) is a cross-sectional study in all German Federal counties conducted by the Institute of German Dentists [Institut der Deutschen Zahnärzte (IDZ)] in 2005 (Micheelis & Schiffner 2006). A stratified multi-stage probability design was applied to sample subjects in two age groups (35–44 and 65–74 years). Individuals from the states constituting former

East Germany were oversampled. Study subjects were selected randomly according to German population registries in a total of 90 municipalities (sample points), which in turn constituted a cluster random sample based on region and degree of urbanization. Overall, 3960 subjects were sampled. After excluding those who were deceased ( $N = 22$ ), emigrated ( $N = 154$ ) or had medical problems ( $N = 142$ ), 3642 subjects were invited. Response rates in the two age groups were 52.1% and 55.7% resulting in 925 adults and 1040 seniors.

### Dental examination

In SHIP-0 and SHIP-Trend, CAL and PD were assessed at the distobuccal, midbuccal, mesiobuccal and midlingual sites using a periodontal probe (SHIP-0: PCP-11; SHIP-TREND: PCP UNC15; Hu-Friedy, Chicago, IL, USA) on a half-mouth basis alternating on the right or left side. Measurements were mathematically rounded to whole millimetres. Third molars were excluded.

In DMS IV, CAL and PD were assessed at the midbuccal, mesiobuccal and distolingual sites at twelve index teeth (17, 16, 11, 24, 26, 27, 31, 36, 37, 47, 46, 44; two-digit notation according to World Dental Federation using a periodontal probe (PCP 11.5 WHO probe, M+W Dental Bidingen, Germany). Third molars were excluded.

### Definition of periodontitis

Three periodontitis case definitions were used. First, according to CDC-AAP Working Group (Page & Eke 2007), severe periodontitis was defined as  $\geq 2$  inter-proximal sites with CAL  $\geq 6$  mm (not on same tooth) and  $\geq 1$  inter-proximal site with PD  $\geq 5$  mm; moderate periodontitis was defined as  $\geq 2$  inter-proximal sites with CAL  $\geq 4$  mm (not on same tooth) or  $\geq 2$  inter-proximal sites with PD  $\geq 5$  mm. Second, according to the 5th European Workshop in Periodontology (EWP) (Tonetti & Claffey 2005), we defined moderate periodontitis as presence of proximal CAL of  $\geq 3$  mm in  $\geq 2$  non-adjacent teeth. Severe periodontitis was defined as presence of proximal CAL of  $\geq 5$  mm in  $\geq 30\%$  of

teeth. Third, we also defined subjects with  $\geq 2$  teeth with interproximal (mesiobuccal or distobuccal) CAL of  $\geq 4$  mm and  $\geq 6$  mm as having moderate and severe periodontitis, respectively, because this definition was used in a previous publication using SHIP data (Dietrich et al. 2009). For the present analysis, total periodontitis comprised moderate and severe periodontitis in all of the three definitions.

In the present study, we restricted the analysis to those with at least two sites with CAL and PD measurements, as both the CDC-AAP and the EWP periodontitis case definition necessitate the presence of at least two teeth (Tonetti & Claffey 2005, Page & Eke 2007). The numbers of those without any periodontal measurements were 567(13.2%), 882(20.8%) and 254(12.9%) for SHIP-0, SHIP-Trend and DMS IV respectively. Of the remaining who underwent a periodontal examination, 277(6.4%), 82(1.9%) and 42(2.1%) subjects had less than two CAL or PD measurements in the three respective studies. After additionally excluding those with missing values of covariates, 3298, 3255 and 1595 subjects were used in the final analysis for SHIP-0, SHIP-Trend and DMS IV respectively.

#### Covariates assessment

For all studies, smoking status was defined as never, former or current smoking. Education level was classified into  $<10$ , 10 and  $>10$  years. Marital status was coded as married, single, divorced and widowed. Body height and weight were determined using calibrated scales. Subjects wore light clothing. Body mass index (BMI) was calculated by kilogram divided by square metres. The BMI was classified into  $<25.0$  kg/m<sup>2</sup>, 25.0–29.9 kg/m<sup>2</sup> and  $>30.0$  kg/m<sup>2</sup>. Self-perceived tooth status was coded as very good, good, satisfactory, less good and poor. Self-reported diabetes was classified as no and yes. Self-reported bad breath was coded as no and yes. The other covariates included: last visit to dentist ( $<7$ , 7–12 or  $>12$  months), dental visit frequency in the last 12 months (0, 1, 2, 3 or  $\geq 4$  times), reasons for last dental visit (precautionary check-up, dental problems or others), tooth brushing

frequency per day ( $\geq 3$  times, twice or  $\leq$  once), usage of other inter-dental cleaning devices (no or yes), self-reported presence of mobile teeth (no or yes) and bleeding on brushing (no, sometimes or often).

#### Statistical analysis

Basic characteristics of the three study samples were shown as mean ( $\pm$  standard deviation) or as numbers (percentages). Survey logistic regression models, taking into account of the sampling design, were applied to build the prediction models. We constructed different models on SHIP-0 data. The full model considered all covariates listed in Table 1. Because age did not fulfil the linearity assumption, age and age-squared were included in the models. Wald tests were used to determine which variables had to be included in the models. All final models included age, gender, smoking status, education level, bleeding on brushing and self-reported presence of mobile teeth as major terms. Interaction terms between the variables were separately evaluated and included if overall  $p$  was  $<0.05$ . Because some of the variables were not recorded in DMS IV, reduced models were built. These included age, gender, smoking status and education level. Again, interaction terms were evaluated.

Harrell's Concordance-statistics (C-statistics), equivalent to area under receiver operating characteristics curve in logistic regression and a modified version of Hosmer–Lemeshow's goodness-of-fit test (Archer & Lemeshow 2006) were used to evaluate model discrimination and calibration. C-statistics between 0.7–0.9 were considered as being moderately useful (Swets 1988). Bootstrap methods were used for internal model validation and over-optimism estimation (Harrell et al. 1996, Steyerberg et al. 2001). Bootstrap analysis was replicated on 200 different samples of the same sample size drawn with replacement from the original sample. Optimism, a measurement of internal model validation, equals the difference between respective statistics of the bootstrap sample and the original sample. Optimism-corrected C-statistics were calculated as C-statistics from the original sample

minus optimism (Harrell et al. 1996, Steyerberg et al. 2001). The optimal cut-off value for predicted probabilities of periodontitis, which was used to distinguish periodontitis cases from healthy subjects, was the one that would maximize Youden's index in SHIP-0. We externally validated full models in SHIP-Trend and reduced models in DMS IV. For validation samples, C-statistics and agreement of actual and predicted prevalences of periodontitis were calculated. All statistical analyses were conducted using Stata/MP 12.1 (StataCorp 2012). A two-sided  $p < 0.05$  was considered statistically significant.

#### Results

Basic characteristics of study subjects are shown in Table 1. In SHIP-0, the average age was  $45.8 \pm 15.0$  years with men comprising 48.4% of the population, while in SHIP-Trend, the average age was  $48.8 \pm 14.6$  years with men comprising 49.0%. In DMS IV, the average age was  $52.7 \pm 14.7$  years and 45.5% were men.

In SHIP-0, the prevalence of total periodontitis was 52.1%, 74.1% and 50.0% according to the CDC-AAP, the EWP and Dietrich's definition respectively (Table 2). Likewise, for SHIP-Trend, prevalences of total periodontitis were 52.0%, 66.0% and 49.7% respectively. In DMS IV, prevalences of total periodontitis for the three definitions were 80.4%, 92.0% and 80.2% respectively. The Kappa values for agreement of different definitions of periodontitis ranged from 0.46 to 0.91 (Tables S1–S3).

#### Model training in SHIP-0 and validation in SHIP-Trend for total periodontitis

The full models included age, gender, smoking, education, bleeding on brushing and self-reported presence of mobile teeth as independent variables (Table 3 and Table S4). For the CDC-AAP definition, the C-statistic [95% confidence interval (CI)] was 0.84 (0.82–0.86) (Table 4). The optimal cut-off value for predicted probabilities of periodontitis was 0.49 with the corresponding sensitivity and specificity being 80.9% and 73.8%. The optimism of internal validation was 0.0014 and the optimism-corrected C-statistic was

Table 1. Basic characteristics of the study subjects in SHIP-0, SHIP-Trend and DMS IV

|  | SHIP-0<br>(n = 3298) | SHIP-Trend<br>(n = 3255) | DMS IV<br>(n = 1595) |
|--|----------------------|--------------------------|----------------------|
| Age (years)                                  | 45.8 ± 15.0          | 48.8 ± 14.6              | 52.7 ± 14.7          |
| Gender                                       |                      |                          |                      |
| Men  | 1596 (48.4)          | 1596 (49.0)              | 726 (45.5)           |
| Women  | 1702 (51.6)          | 1659 (51.0)              | 869 (54.5)           |
| BMI (kg/m <sup>2</sup> )                     |                      |                          |                      |
| <25.0  | 1229 (37.3)          | 1042 (32.0)              | 698 (43.9)           |
| ≥25.0–<30.0                                  | 1291 (39.1)          | 1296 (39.9)              | 617 (38.8)           |
| ≥30.0  | 778 (23.6)           | 914 (28.1)               | 276 (17.3)           |
| Marital status                               |                      |                          |                      |
| Married                                      | 2184 (66.2)          | 2069 (63.6)              |                      |
| Single                                       | 713 (21.6)           | 787 (24.2)               |                      |
| Divorced                                     | 252 (7.6)            | 265 (8.1)                |                      |
| Widowed                                      | 149 (4.5)            | 134 (4.1)                |                      |
| Education level                              |                      |                          |                      |
| <10 years                                    | 1025 (31.1)          | 538 (16.5)               | 637 (39.9)           |
| 10 years                                     | 1647 (49.9)          | 1790 (55.0)              | 508 (31.9)           |
| >10 years                                    | 626 (19.0)           | 927 (28.5)               | 450 (28.2)           |
| Smoking status                               |                      |                          |                      |
| Never  | 1182 (35.8)          | 1215 (37.3)              | 841 (52.7)           |
| Former                                       | 1052 (31.9)          | 871 (26.8)               | 355 (22.3)           |
| Current                                      | 1064 (32.3)          | 1169 (35.9)              | 399 (25.0)           |
| Bleeding on brushing                         |                      |                          |                      |
| No   | 1931 (58.6)          | 1742 (53.5)              |                      |
| Sometimes                                    | 1197 (36.3)          | 1383 (42.5)              |                      |
| Often  | 170 (5.2)            | 130 (4.0)                |                      |
| Self-reported presence of mobile teeth       |                      |                          |                      |
| No   | 2904 (88.0)          | 2936 (90.2)              |                      |
| Yes  | 394 (12.0)           | 319 (9.8)                |                      |
| Self-perceived tooth status                  |                      |                          |                      |
| Very good                                    | 145 (4.4)            | 215 (6.6)                | 54 (3.4)             |
| Good   | 1228 (37.2)          | 1405 (43.2)              | 574 (36.0)           |
| Satisfactory                                 | 1316 (39.9)          | 1130 (34.7)              | 687 (43.1)           |
| Less good                                    | 431 (13.1)           | 356 (10.9)               | 211 (13.2)           |
| Poor   | 178 (5.4)            | 149 (4.6)                | 68 (4.3)             |
| Self-reported diabetes                       |                      |                          |                      |
| No   | 3112 (94.4)          | 3012 (92.5)              |                      |
| Yes  | 186 (5.6)            | 243 (7.5)                |                      |
| Self-reported bad breath                     |                      |                          |                      |
| No   | 2584 (78.4)          | 2551 (78.4)              |                      |
| Yes  | 714 (21.7)           | 704 (21.6)               |                      |
| Time from last visit to dentist              |                      |                          |                      |
| <7 months                                    | 2341 (71.0)          | 2249 (69.1)              |                      |
| 7–12 months                                  | 623 (18.9)           | 693 (21.3)               |                      |
| >12 months                                   | 334 (10.1)           | 311 (9.6)                |                      |
| Dental visit frequency in the last 12 months |                      |                          |                      |
| 0  | 334 (10.1)           | 0 (0.0)                  |                      |
| 1  | 675 (20.5)           | 882 (30.2)               |                      |
| 2  | 1096 (33.2)          | 1088 (37.3)              |                      |
| 3  | 409 (12.4)           | 380 (13.0)               |                      |
| ≥4   | 784 (23.8)           | 570 (19.5)               |                      |
| Reasons for last dental visit                |                      |                          |                      |
| Precautionary check-up                       | 1670 (50.6)          | 1184 (36.6)              |                      |
| Dental problems                              | 1166 (35.4)          | 1767 (54.7)              |                      |
| Others                                       | 462 (14.0)           | 281 (8.7)                |                      |
| Tooth brushing frequency per day             |                      |                          |                      |
| ≥3 times                                     | 278 (7.4)            | 206 (6.3)                |                      |
| twice  | 2486 (75.4)          | 2578 (79.2)              |                      |
| ≤once  | 534 (16.2)           | 474 (14.5)               |                      |
| Usage of other inter-dental care devices     |                      |                          |                      |
| No   | 2023 (61.3)          | 1554 (47.7)              |                      |
| Yes  | 1275 (39.7)          | 1701 (52.3)              |                      |

Data are presented as mean ± standard deviation or numbers (percentages). BMI, body mass index.

0.84. In terms of external model validation in SHIP-Trend, the C-statistic was 0.82. Predicted prevalence of total periodontitis was 66.2%; the agreement of actual and predicted prevalence was 72.8%. For the EWP definition, the C-statistic (95% CI) was 0.82 (0.80–0.84), and the optimal cut-off value was 0.75 and corresponding values for sensitivity and specificity were 73.5% and 74.9%. The optimism of internal validation was 0.0025 with an optimism-corrected C-statistic of 0.81. As for external validation, the C-statistic, predicted prevalence and agreement were 0.81, 72.9% and 75.5% respectively. For the Dietrich et al. definition, the C-statistic (95% CI) was 0.85 (0.83–0.86). The optimal cut-off value was 0.45 and the corresponding values of sensitivity and specificity were 82.6% and 72.6% respectively. The optimism of internal validation and corrected C-statistic were 0.0028 and 0.85. Regarding the external validation, the C-statistic, predicted prevalence and agreement were 0.82, 67.2% and 71.3% respectively. All *p* values of goodness-of-fit test for the model calibration were >0.05 (Table 4).

#### Model training in SHIP-0 and validation in DMS IV for total periodontitis

The reduced models included age, gender, smoking and education as independent variables (Table 5 and Table S5). For the CDC-AAP definition, the C-statistic (95% CI) was 0.82 (0.81–0.84) (Table S6). The cut-off value of probability of periodontitis was 0.51 with the corresponding sensitivity and specificity of 79.0% and 73.2%. The optimism of internal validation was 0.0007 and optimism-corrected C-statistic was 0.82. In terms of external model validation, the C-statistic was 0.72, predicted prevalence of total periodontitis was 67.8%, the agreement of actual and predicted prevalence in DMS IV was 71.4%. For the EWP definition, the C-statistic (95% CI) was 0.81 (0.80–0.83) and cut-off value of *p* was 0.76 with sensitivity and specificity of 72.4% and 74.8%. The optimism of internal validation was 0.0011 with optimism-corrected C-statistic of 0.81. As for external validation, the C-statistic, predicted prevalence and

Table 2. Prevalence of Periodontitis according to three different case definitions in SHIP-0, SHIP-Trend and DMS IV, [*n* (%)]

| Study      | Periodontitis | CDC-AAP     | EWP definition | Dietrich et al. (2009) |
|------------|---------------|-------------|----------------|------------------------|
| SHIP-0     | No or mild    | 1475 (44.7) | 797 (24.2)     | 1542 (46.8)            |
|            | Moderate      | 1165 (35.3) | 1506 (45.7)    | 968 (29.4)             |
|            | Severe        | 658 (20.0)  | 995 (30.2)     | 788 (23.9)             |
| SHIP-Trend | No or mild    | 1563 (48.0) | 1108 (34.0)    | 1637 (50.3)            |
|            | Moderate      | 1142 (35.1) | 1297 (39.9)    | 963 (29.6)             |
|            | Severe        | 550 (16.9)  | 850 (26.1)     | 655 (20.1)             |
| DMS IV     | No or mild    | 304 (19.1)  | 122 (7.6)      | 306 (19.2)             |
|            | Moderate      | 815 (51.1)  | 708 (44.4)     | 669 (41.9)             |
|            | Severe        | 476 (29.8)  | 765 (48.0)     | 620 (39.0)             |

CDC-AAP, Center for Disease Control and Prevention-American Academy of Periodontology; EWP, European Workshop in Periodontology.

Table 3. Logistic regression coefficients (standard error) of full models for three periodontal case definitions (total periodontitis) based on SHIP-0

|   | Model 1        | Model 2        | Model 3        |
|---|----------------|----------------|----------------|
| Intercept   | -7.444 (0.586) | -4.405 (0.551) | -7.953 (0.598) |
| Age   |                |                |                |
| Age   | 0.249 (0.023)  | 0.229 (0.0239) | 0.260 (0.0234) |
| Age <sup>2</sup>  | -0.002 (0.001) | -0.002 (0.001) | -0.002 (0.001) |
| Smoking (reference: never)  |                |                |                |
| former  | 0.910 (0.126)  | 0.532 (0.133)  | 0.860 (0.128)  |
| current   | 0.206 (0.130)  | 0.0626 (0.130) | 0.179 (0.130)  |
| Education(reference: < 10 years)                                      |                |                |                |
| 10 years  | -0.403 (0.147) | -1.221 (0.254) | -0.337 (0.150) |
| >10 years   | -0.858 (0.161) | -1.551 (0.283) | -0.779 (0.163) |
| Gender(reference: men)  |                |                |                |
| women   | -0.462 (0.106) | -1.450 (0.283) | -0.521 (0.113) |
| Bleeding on brushing(reference: no)                                   |                |                |                |
| often   | 1.250 (0.294)  | 1.017 (0.283)  | 1.275 (0.293)  |
| sometimes   | 0.496 (0.114)  | 0.297 (0.108)  | 0.482 (0.117)  |
| Self-reported presence of mobile teeth (reference: no)                |                |                |                |
| yes   | 1.402 (0.186)  | 1.090 (0.253)  | 1.058 (0.251)  |
| Interaction between gender and self-reported presence of mobile teeth |                |                |                |
| women × yes   | -              | -              | 0.806 (0.362)  |
| Interaction between gender and education                              |                |                |                |
| women × 10 years  | -              | 1.320 (0.307)  | -              |
| women × >10 years   | -              | 1.265 (0.342)  | -              |

The following periodontal case definitions were modelled in logistic regression analyses: Model 1: CDC-AAP; Model 2: EWP; Model 3: Dietrich et al.

agreement were 0.78, 74.4% and 76.2% respectively. For the Dietrich et al. definition, the C-statistic (95% CI) was 0.83 (0.81–0.85). The cut-off value of *p* was 0.48 and the corresponding sensitivity and specificity were 80.0% and 72.7%. The optimism of internal validation and corrected C-statistic were 0.0005 and 0.83. Regarding the external validation, the C-statistic, predicted prevalence, and agreement were 0.72, 67.4% and 71.3% respectively. All *p* values of goodness-of fit-test for the model calibration were >0.05 (Table 4).

#### Model training in SHIP-0 and validation in SHIP-Trend and DMS IV for severe periodontitis

We additionally modelled severe periodontitis in SHIP-0 and validated these models in SHIP-Trend and DMS IV. Variables and coefficients were presented in Tables S6 and S9 for full models and Tables S8 and S10 for reduced models. As shown in Table S7, the C-statistics for the full models were 0.84 (0.82–0.86), 0.88 (0.86–0.89) and 0.85 (0.83–0.86) for CDC-AAP, EWP and Dietrich's definition of severe periodontitis respectively, while the

corresponding C-statistics of the reduced models for the three definitions of severe periodontitis were 0.79 (0.77–0.81), 0.84 (0.83–0.86) and 0.84 (0.83–0.86).

#### Discussion

In the present study, we developed several population prevalence prediction models for total and severe periodontitis in SHIP-0 and externally validated them in SHIP-Trend and DMS IV, both of which were community-based surveys. We found that the models based on self-reported measures had a good calibration and discrimination with C-statistics ranging between 0.79 and 0.85. This suggested that the model performance was moderate and the models to assess periodontitis might be useful in community-based periodontitis studies.

Until now, several research groups have developed prediction rules for periodontitis using self-reported questions, but their questions and the performance of prediction models varied across different study populations. The self-reported questions used in the CDC Periodontal Disease Surveillance Project covered eight items, all of which pertained to the periodontal health status (Eke & Genco 2007). Other questionnaires were developed and evaluated in studies from New York (Genco et al. 2007), Florida (Gilbert & Litaker 2007), Australia (Slade 2007) and Brazil (Cyrino et al. 2011), but models developed from these studies were seldom validated in another study. In contrast, Dietrich et al. developed a prediction model for periodontitis in a German practice-based sample (Dietrich et al. 2005), and validated it in an external German community-based sample (Dietrich et al. 2009) and others have validated it in a Chinese clinical sample (Wu et al. 2013). However, because the model from Dietrich et al. was developed using clinical rather than community-based data, it may be much more suitable for periodontal diseases studies in clinics than periodontitis surveillance in community-based populations.

An approach for predicting the population prevalence of periodontitis in communities is multivariable modelling of self-reported items combining demographic characteris-

Table 4. Performance of the models for total periodontitis

|  | CDC-AAP          | EWP              | Dietrich et al.  |
|--|------------------|------------------|------------------|
| Results for the validation of reduced models derived from SHIP-0 in SHIP-Trend |                  |                  |                  |
| C-statistics (95% CI)  | 0.84 (0.82–0.86) | 0.82 (0.80–0.84) | 0.85 (0.83–0.86) |
| Sensitivity (95% CI),%   | 80.9 (80.6–81.2) | 73.5 (73.2–73.8) | 82.6 (82.3–82.9) |
| Specificity (95% CI),%   | 73.8 (73.4–74.1) | 74.9 (74.5–75.4) | 72.6 (72.3–73.0) |
| Positive predictive value (95% CI),%   | 77.1 (76.8–77.4) | 89.4 (89.1–89.6) | 75.1 (74.8–75.4) |
| Negative predictive value (95% CI),%   | 78.0 (77.7–78.4) | 49.7(49.2–50.1)  | 80.7 (80.4–81.0) |
| Cut-off value of probability   | 0.49             | 0.75             | 0.45             |
| Optimism   | 0.0014           | 0.0025           | 0.0028           |
| Optimism-corrected C-statistics  | 0.84             | 0.82             | 0.85             |
| p value of goodness-of-fit test  | 0.96             | 0.80             | 0.96             |
| C-statistics (95% CI) in SHIP-Trend  | 0.82 (0.81–0.83) | 0.81 (0.79–0.82) | 0.82 (0.81–0.83) |
| Observed prevalence in SHIP-Trend  | 52.0%            | 66.0%            | 49.7%            |
| Predicted prevalence in SHIP-Trend   | 66.2%            | 72.9%            | 67.2%            |
| Agreement between observed and predicted prevalence in SHIP-Trend              | 72.8%            | 75.5%            | 71.3%            |
| Results for the validation of reduced models derived from SHIP-0 in DMS IV     |                  |                  |                  |
| C-statistics (95% CI)  | 0.82 (0.81–0.84) | 0.81 (0.80–0.83) | 0.83 (0.81–0.85) |
| Sensitivity (95% CI),%   | 79.0 (78.7–79.4) | 72.4 (72.1–72.7) | 80.0 (79.7–80.3) |
| Specificity (95% CI),%   | 73.2 (72.9–73.6) | 74.8 (74.4–75.3) | 72.7 (72.4–73.1) |
| Positive predictive value (95% CI),%   | 76.3 (76.0–76.6) | 89.2 (89.0–89.4) | 74.6 (74.2–74.9) |
| Negative predictive value(95% CI),%  | 76.2 (75.9–76.6) | 48.7 (48.2–49.1) | 78.5 (78.1–78.8) |
| Cut-off value of probability   | 0.51             | 0.76             | 0.48             |
| Optimism   | 0.0007           | 0.0011           | 0.0005           |
| Optimism-corrected C-statistics  | 0.82             | 0.81             | 0.83             |
| p value of goodness-of-fit test  | 0.38             | 0.87             | 0.61             |
| C-statistics (95% CI) in DMS IV  | 0.72 (0.69–0.76) | 0.78 (0.73–0.82) | 0.72 (0.69–0.76) |
| Observed prevalence in DMS IV  | 80.9%            | 92.4%            | 80.8%            |
| Predicted prevalence in DMS IV   | 67.8%            | 74.4%            | 67.4%            |
| Agreement between observed and predicted prevalence in DMS IV                  | 71.4%            | 76.2%            | 71.3%            |

CDC-AAP, Center for Disease Control and Prevention-American Academy of Periodontology; EWP, European Workshop in Periodontology.

Table 5. Logistic regression coefficients (standard error) of full models with a reduced number of predictors for three periodontal case definitions (total periodontitis) based on SHIP-0

|  | Model 4        | Model 5        | Model 6        |
|--|----------------|----------------|----------------|
| Intercept                                | -7.187 (0.581) | -4.244 (0.536) | -7.751 (0.601) |
| Age                                      |                |                |                |
| Age                                      | 0.259 (0.023)  | 0.235 (0.023)  | 0.272 (0.023)  |
| Age <sup>2</sup>                         | -0.002 (0.001) | -0.002 (0.001) | -0.002 (0.001) |
| Smoking (reference: never)               |                |                |                |
| Former                                   | 0.247 (0.132)  | 0.092 (0.129)  | 0.223 (0.131)  |
| Current                                  | 0.776 (0.118)  | 0.459 (0.128)  | 0.729 (0.120)  |
| Education(reference: <10 years)          |                |                |                |
| 10 years                                 | -0.425 (0.144) | -1.243 (0.250) | -0.353 (0.146) |
| >10 years                                | -0.886 (0.159) | -1.620 (0.279) | -0.799 (0.161) |
| Gender(reference: men)                   |                |                |                |
| Women                                    | -0.404 (0.105) | -1.427 (0.280) | -0.405 (0.108) |
| Interaction between gender and education |                |                |                |
| Women × 10 years                         | -              | 1.315 (0.306)  | -              |
| Women × >10 years                        | -              | 1.297 (0.338)  | -              |

The following periodontal case definitions were modelled in logistic regression analyses: Model 4: CDC-AAP; Model 5: EWP; Model 6: Dietrich et al.

tics with periodontitis symptoms. In the present study, we derived several more sophisticated models from SHIP-0 including age, gender, smoking status, self-reported tooth mobility, education level and bleeding on brushing. Most of the variables were regarded as risk factors of or signs and symptoms of periodontitis (Genco & Borgnakke 2013). Consistent with previous research results (Dietrich et al. 2009), we included age, smoking and self-reported tooth mobility. Nevertheless, we considered more potential variables to be selected for model development.

Previous studies showed that gender was of paramount importance in the prevalence of periodontitis (Shiau & Reynolds 2010a) and differential gene regulation may biologically contribute to the gender differences in periodontal disease (Shiau & Reynolds 2010b). Like most chronic diseases, education as a proxy for the socioeconomic status was also shown to be a predictor of periodontitis (Boillot et al. 2011, Gorman et al. 2012). Self-reported bleeding on brushing was predictive of periodontitis here. Consistently, similar items were predictive in previous studies: bleeding gums was included in the final models of the MI-Perio Study and the Erie County Study (Genco et al. 2007), while self-rating of gum health was considered in the Florida Dental Care Study (Gilbert & Litaker 2007). Some other self-reported measurements were also considered as candidate variables in the present study. However, they did not show significant improvements for model performance and were not included in the final models.

The C-statistics and agreements of actual and predicted prevalence of periodontitis differ between SHIP-Trend and DMS IV. The difference might be due to several factors. First, the source population of SHIP-0 is similar to that of SHIP-Trend, while different from that of DMS IV. The distribution of age, gender, education level and smoking status were different in SHIP-Trend and DMS IV as shown in Table 1. Thus, better prediction in similar population *versus* worse prediction in a more different population may be expected. Second, the models for validation in DMS IV are reduced due to the fact that two vari-

ables (bleeding when brushing and self-reported presence of mobile teeth) were not available in DMS IV. The models developed for validation in SHIP-Trend are more complex and resulted in better model performance for validation. Third, the predicted prevalence and agreement between actual and predicted prevalence are largely dependent on the cut-off value of probability and periodontal recording protocols, which were different in SHIP-Trend and DMS IV.

Our results demonstrated that the prevalence prediction models which we developed would be a promising periodontitis surveillance instrument for the German community-based population. In the first place, internal validation analysis was conducted to avoid over-fitting of the prediction models. Bootstrap methods were used to estimate the over-optimism, and the optimism-corrected c-statistics were still moderately useful. Next, external validation analysis was performed in two different populations, both of which were also community-based studies. The source population of our model training sample, SHIP-0, was similar to that of SHIP-Trend, while different to that of DMS IV. The results of the two external validation analyses ascertained the performance of our prediction models. This is a strength of our study. Finally, we used three kinds of definitions of periodontitis to evaluate whether different definitions had major impact on our models. As shown in Tables 3 and 4, the implications of how to define periodontitis were negligible and changes in C-statistics were minor. Although the EWP periodontitis definition was originally intended for risk factor research (Tonetti & Claffey 2005), it was still included in our present study due to its usage in many studies (Matuliene et al. 2008, Eke et al. 2012).

We do acknowledge that our study has some limitations. In none of the three surveys used in the present study, periodontal measurements were based on full-mouth periodontal examinations at six sites per tooth. Thus, the true prevalence of total periodontitis was underestimated (Thomson & Williams 2002). Second, the prediction models proposed in this study were developed

for the population periodontitis prevalence and surveillance. The models are not encouraged to be used in clinical practice.

In conclusion, we developed several models based on self-reported questions and demographic characteristics that moderately predicted the population periodontitis prevalence. Prediction models were successfully validated in two separate samples from different periods or different regions and showed a moderate discriminatory power. With regard to public health issues, these findings may be helpful to assess periodontitis prevalence and surveillance and to track susceptible populations. In the future, the proposed models should be validated in various community-based contexts to evaluate their external performance.

## References

- Archer, K. & Lemeshow, S. (2006) Goodness-of-fit test for a logistic regression model fitted using survey sample data. *The Stata Journal* **6**, 97–105.
- Blicher, B., Josphipura, K. & Eke, P. (2005) Validation of self-reported periodontal disease: a systematic review. *Journal of Dental Research* **84**, 881–890.
- Boillot, A., El Halabi, B., Batty, G. D., Range, H., Czernichow, S. & Boucard, P. (2011) Education as a predictor of chronic periodontitis: a systematic review with meta-analysis population-based studies. *PLoS ONE* **6**, e21508.
- Chambrone, L., Guglielmetti, M. R., Pannuti, C. M. & Chambrone, L. A. (2011) Evidence grade associating periodontitis to preterm birth and/or low birth weight: I. A systematic review of prospective cohort studies. *Journal of Clinical Periodontology* **38**, 795–808.
- Cyrino, R. M., Miranda Cota, L. O., Pereira Lages, E. J., Bastos Lages, E. M. & Costa, F. O. (2011) Evaluation of self-reported measures for prediction of periodontitis in a sample of Brazilians. *Journal of Periodontology* **82**, 1693–1704.
- Dietrich, T., Kaiser, W., Naumann, M., Stosch, U., Schwahn, C., Biffar, R., Dietrich, D. & Kocher, T. (2009) Validation of a multivariate prediction rule for history of periodontitis in a separate population. *Journal of Clinical Periodontology* **36**, 493–497.
- Dietrich, T., Sharma, P., Walter, C., Weston, P. & Beck, J. (2013) The epidemiological evidence behind the association between periodontitis and incident atherosclerotic cardiovascular disease. *Journal of Clinical Periodontology* **40** (Suppl 14), S70–S84.
- Dietrich, T., Stosch, U., Dietrich, D., Kaiser, W., Bernimoulin, J. P. & Josphipura, K. (2007) Prediction of periodontal disease from multiple self-reported items in a German practice-based sample. *Journal of Periodontology* **78**, 1421–1428.
- Dietrich, T., Stosch, U., Dietrich, D., Schamberger, D., Bernimoulin, J. P. & Josphipura, K. (2005) The accuracy of individual self-reported items to determine periodontal disease history. *European Journal of Oral Sciences* **113**, 135–140.
- Eke, P. I., Dye, B. A., Wei, L., Slade, G. D., Thornton-Evans, G. O., Beck, J. D., Taylor, G. W., Borgnakke, W. S., Page, R. C. & Genco, R. J. (2013) Self-reported measures for surveillance of periodontitis. *Journal of Dental Research* **92**, 1041–1047.
- Eke, P. I., Dye, B. A., Wei, L., Thornton-Evans, G. O. & Genco, R. J. (2012) Prevalence of periodontitis in adults in the United States: 2009 and 2010. *Journal of Dental Research* **91**, 914–920.
- Eke, P. I. & Genco, R. J. (2007) CDC Periodontal Disease Surveillance Project: background, objectives, and progress report. *Journal of Periodontology* **78**, 1366–1371.
- Engelbreton, S. & Kocher, T. (2013) Evidence that periodontal treatment improves diabetes outcomes: a systematic review and meta-analysis. *Journal of Clinical Periodontology* **40** (Suppl 14), S153–S163.
- Genco, R. J. & Borgnakke, W. S. (2013) Risk factors for periodontal disease. *Periodontol 2000* **62**, 59–94.
- Genco, R. J., Falkner, K. L., Grossi, S., Dunford, R. & Trevisan, M. (2007) Validity of self-reported measures for surveillance of periodontal disease in two western New York population-based studies. *Journal of Periodontology* **78**, 1439–1454.
- Gilbert, G. H. & Litaker, M. S. (2007) Validity of self-reported periodontal status in the Florida dental care study. *Journal of Periodontology* **78**, 1429–1438.
- Gorman, A., Kaye, E. K., Apovian, C., Fung, T. T., Nunn, M. & Garcia, R. I. (2012) Overweight and obesity predict time to periodontal disease progression in men. *Journal of Clinical Periodontology* **39**, 107–114.
- Harrell, F. E. Jr, Lee, K. L. & Mark, D. B. (1996) Multivariable prognostic models: issues in developing models, evaluating assumptions and adequacy, and measuring and reducing errors. *Statistics in Medicine* **15**, 361–387.
- Hensel, E., Gesch, D., Biffar, R., Bernhardt, O., Kocher, T., Splieth, C., Born, G. & John, U. (2003) Study of Health in Pomerania (SHIP): a health survey in an East German region. Objectives and design of the oral health section. *Quintessence International* **34**, 370–378.
- Holtfreter, B., Kocher, T., Hoffmann, T., Desvarieux, M. & Micheelis, W. (2010) Prevalence of periodontal disease and treatment demands based on a German dental survey (DMS IV). *Journal of Clinical Periodontology* **37**, 211–219.
- Ide, M. & Papapanou, P. N. (2013) Epidemiology of association between maternal periodontal disease and adverse pregnancy outcomes—systematic review. *Journal of Clinical Periodontology* **40** (Suppl 14), S181–S194.
- Josphipura, K. J., Douglass, C. W., Garcia, R. I., Valachovic, R. & Willett, W. C. (1996) Validity of a self-reported periodontal disease measure. *Journal of Public Health Dentistry* **56**, 205–212.
- Lalla, E. & Papapanou, P. N. (2011) Diabetes mellitus and periodontitis: a tale of two common interrelated diseases. *Nature Reviews Endocrinology* **7**, 738–748.
- Matuliene, G., Pjetursson, B. E., Salvi, G. E., Schmidlin, K., Bragger, U., Zwahlen, M. & Lang, N. P. (2008) Influence of residual pockets on progression of periodontitis and tooth loss: results after 11 years of maintenance. *Journal of Clinical Periodontology* **35**, 685–695.

- Micheelis, W. & Schiffner, U. (2006) *Vierte Deutsche Mundgesundheitsstudie (DMS IV). Neue Ergebnisse zu oralen Erkrankungsprävalenzen, Risikogruppen und zum zahnärztlichen Versorgungsgrad in Deutschland 2005*. Köln: Deutscher Zahnärzte Verlag.
- Page, R. C. & Eke, P. I. (2007) Case definitions for use in population-based surveillance of periodontitis. *Journal of Periodontology* **78**, 1387–1399.
- Shiau, H. J. & Reynolds, M. A. (2010a) Sex differences in destructive periodontal disease: a systematic review. *Journal of Periodontology* **81**, 1379–1389.
- Shiau, H. J. & Reynolds, M. A. (2010b) Sex differences in destructive periodontal disease: exploring the biologic basis. *Journal of Periodontology* **81**, 1505–1517.
- Slade, G. D. (2007) Interim analysis of validity of periodontitis screening questions in the Australian population. *Journal of Periodontology* **78**, 1463–1470.
- StataCorp (2012) *Stata Statistical Software: Release 12*. College Station, TX: StataCorp LP.
- Steyerberg, E. W., Harrell, F. E. Jr, Borsboom, G. J., Eijkemans, M. J., Vergouwe, Y. & Habbema, J. D. (2001) Internal validation of predictive models: efficiency of some procedures for logistic regression analysis. *Journal of Clinical Epidemiology* **54**, 774–781.
- Swets, J. A. (1988) Measuring the accuracy of diagnostic systems. *Science* **240**, 1285–1293.
- Thomson, W. M. & Williams, S. M. (2002) Partial- or full-mouth approaches to assessing the prevalence of and risk factors for periodontal disease in young adults. *Journal of Periodontology* **73**, 1010–1014.
- Tonetti, M. S. & Claffey, N. (2005) Advances in the progression of periodontitis and proposal of definitions of a periodontitis case and disease progression for use in risk factor research. Group C consensus report of the 5th European Workshop in Periodontology. *Journal of Clinical Periodontology* **32**(Suppl 6), 210–213.
- Volzke, H., Alte, D., Schmidt, C. O., Radke, D., Lorbeer, R., Friedrich, N., Aumann, N., Lau, K., Piontek, M., Born, G., Havemann, C., Itermann, T., Schipf, S., Haring, R., Baumeister, S. E., Wallaschofski, H., Nauck, M., Frick, S., Arnold, A., Junger, M., Mayerle, J., Kraft, M., Lerch, M. M., Dorr, M., Reffelmann, T., Empen, K., Felix, S. B., Obst, A., Koch, B., Glaser, S., Ewert, R., Fietze, I., Penzel, T., Doren, M., Rathmann, W., Haerting, J., Hannemann, M., Ropcke, J., Schminke, U., Jurgens, C., Tost, F., Rettig, R., Kors, J. A., Ungerer, S., Hegenscheid, K., Kuhn, J. P., Kuhn, J., Hosten, N., Puls, R., Henke, J., Gloger, O., Teumer, A., Homuth, G., Volker, U., Schwahn, C., Holtfreter, B., Polzer, I., Kohlmann, T., Grabe, H. J., Rosskopf, D., Kroemer, H. K., Kocher, T., Biffar, R., John, U. & Hoffmann, W. (2011) Cohort profile: the study of health in Pomerania. *International Journal of Epidemiology* **40**, 294–307.
- Wu, X., Weng, H. & Lin, X. (2013) Self-reported questionnaire for surveillance of periodontitis in Chinese patients from a prosthodontic clinic: a validation study. *Journal of Clinical Periodontology* **40**, 616–623.

### Supporting Information

Additional Supporting Information may be found in the online version of this article:

**Table S1.** Cross tabulation of different periodontitis case definitions in SHIP-0.

**Table S2.** Cross tabulation of different periodontitis case definitions in SHIP-Trend.

**Table S3.** Cross tabulation of different periodontitis case definitions in DMS IV.

**Table S4.** Odds ratio and 95% confidence interval of full models for three periodontal case definitions (moderate plus severe periodontitis) based on SHIP-0.

**Table S5.** Odds ratio and 95% confidence interval of full models with a reduced number of predictors for three periodontal case definitions (moderate plus severe periodontitis) based on SHIP-0.

**Table S6.** Logistic regression coefficients (standard error) of full models for three periodontal case definitions (severe periodontitis) based on SHIP-0.

**Table S7.** Performance of the models for severe periodontitis.

**Table S8.** Logistic regression coefficients (standard error) of full models with a reduced number of predictors for three periodontal case definitions (severe periodontitis) based on SHIP-0.

**Table S9.** Odds ratio and 95% confidence interval of full models for three periodontal case definitions (Severe periodontitis only) based on SHIP-0.

**Table S10.** Odds ratio and 95% confidence interval of reduced models for three periodontal case definitions (Severe periodontitis only) based on SHIP-0.

Address:

Thomas Kocher

Unit of Periodontology

Dental School

University Medicine

Ernst-Moritz-Arndt University Greifswald

Rotgerberstr. 8

17475 Greifswald

Germany

E-mail: kocher@uni-greifswald.de

### Clinical Relevance

*Scientific rationale for the study:* Self-reported measurements of periodontitis and demographic characteristics might be useful for epidemiological screening for periodontitis.

*Principle findings:* Models consisting age, gender, education, smoking, bleeding on brushing and self-reported presence of mobile teeth were developed, validated and moderately useful for periodontitis in dif-

ferent population-based German populations.

*Practical implications:* The models we developed were useful for periodontitis screening and surveillance in German population.