

Risk calculation and periodontal outcomes

RAUL I. GARCIA, MARTHA E. NUNN & THOMAS DIETRICH

Introduction

Over the past three decades, there has been an extraordinary growth in knowledge regarding our understanding of the biologic and behavioral factors responsible for periodontal disease initiation, progression and response to treatment (28). As this evidence base has grown, a concomitant interest has developed in finding means by which to translate this knowledge effectively into the care of the individual patient (10). Thus, a more detailed and comprehensive assessment of a patient's risk characteristics would appear to be essential to calculate individual risk more accurately, formulate prognoses and make informed treatment decisions (43). However, there exist important conceptual and practical limitations regarding the utility of risk calculation in clinical decision-making at the level of the individual patient.

We will focus our attention, in this topical review, on the value and limitations of the use of periodontal risk determinants, and thus the calculation of risk, in clinical decision-making. In order to do so, we will also aim to address the question of how useful risk factors are in predicting clinical events and outcomes (e.g. disease progression, therapeutic success) for individual patients. In doing so, we will draw on examples from periodontal research as well as from the general medical research literature. We will also briefly discuss periodontal risk factors and the use of risk determinants in screening for periodontal disease in populations. We will aim to show that despite their limitations, screening tools and risk calculators are at least of value in the context of raising public awareness and also as tools for fostering patient education about periodontal health and disease outcomes.

Risk assessment and prognosis

The role of risk factors and risk assessment in the prediction of clinical periodontal outcomes has been a subject of much interest (8, 17, 25, 28, 42). In fact, the assessment of risk, and its use in clinical care, has recently been the focus of an American Academy of Periodontology Task Force (2). In critically assessing the topic, it is important to bear in mind that our knowledge about periodontal risk factors, and the magnitude of their roles, has come primarily from published epidemiologic and clinical research. In her review of periodontal risk factors, Nunn (28) has defined risk factor as 'any characteristic, behavior, or exposure with an association to a particular disease. The relationship is not necessarily causal in nature. ... Some risk factors, if causal, can be modified to reduce one's risk of initiation or progression of disease, such as smoking or improved oral hygiene... while other factors cannot be modified, such as genetic factors.' However, the definition of what is a 'risk factor' is not universally agreed upon. For example, some limit the use of the term 'risk factor' strictly to denote a causal factor and use other terms such as 'risk markers' for noncausal factors or for those not yet proven to be causal factors.

Our understanding, and quantification, of risk for any given disease is based on an assessment of probabilities. In a group or population, this would represent an average risk or incidence proportion (36) and may be expressed as the proportion or percentage of persons expected to experience the condition. Similarly, as applied to an individual patient, risk may be expressed as the probability or likelihood that the person will develop the disease or have it progress to a measurable outcome. Importantly, the quantification of risk for either a population or an

individual also requires that risk to be related to a specific time interval. As Rothman (36) has noted, 'the only way to interpret risk is to know the length of the time period over which the risk applies. This time period may be short or long, but without identifying it, risk values are not meaningful.' Similarly, when using risk calculation to describe prognosis, it is essential that the likelihood of the future outcomes of alternative treatment options be framed in the context of clearly identified time periods.

Prognosis may be defined as the 'likely course and outcome of a disease' (26), and a prognostic factor is any characteristic that relates to the likelihood of success or survival (16). In periodontal disease, prognostic factors can be both risk factors related to the development and progression of disease (e.g. cigarette smoking) as well as manifestations of the disease itself (e.g. the presence of a clinical or radiographic furcation involvement). They may also represent factors that are not directly causally related to the disease but that are surrogate markers or indicators. In clinical dentistry, prognosis is routinely used, whether consciously or unconsciously, by practitioners, third-party payers and patients in the development, adoption and implementation of dental treatment plans. For instance, third-party payers will often restrict payment for certain procedures that are repeated within a 5-year period (e.g., crowns, fixed and removable prostheses, etc.). Implicit in restrictions on payments of this type is the expectation of treatment 'success' for a certain minimum period of time.

While there has been much research on periodontal risk factors, there has been somewhat less research focused specifically on the area of periodontal prognostic indicators. In part, this has been a result of the challenges of conducting long-term, multi-year studies that follow the course of alternate treatment choices. However, a notable series of studies were conducted by McGuire & Nunn (22-24) that investigated the relationship of commonly used clinical parameters to assigned periodontal prognosis, and the relationship of periodontal prognosis and commonly used clinical parameters to tooth loss from periodontal disease, with up to 15 years of follow-up available. They used the technique of multivariate survival analysis to fit a multiple survival regression model for predicting tooth loss as a result of periodontal disease. Based on multivariate survival analysis, initial probing depth, initial furcation involvement, initial mobility, initial percentage bone loss, the presence of a parafunctional habit without a biteguard, smoking and assigned prognosis were all

significantly associated with tooth loss from periodontal disease. However, multivariate survival analysis also demonstrated that assigned prognosis alone did not accurately predict tooth loss from periodontal disease and commonly used clinical parameters did not completely explain tooth loss from periodontal disease.

In a study of periodontal prognostic indicators by Machtei et al. (21), the relationship of prognostic factors to clinical attachment loss and alveolar bone loss was explored in a longitudinal study. Smokers demonstrated greater loss of attachment and greater bone loss than nonsmokers. In addition, baseline probing depth, baseline attachment level and baseline crestal bone height were all significant predictors of attachment loss over time and also of alveolar bone loss over time.

Clinicians and patients would each have clearly much to gain if the risk of disease occurrence and progression, and the probability of the individual patient's prognosis, could be precisely determined. Based on such accurate prognostication, clinicians could recommend with greater scientific precision the most effective treatment plan to their patients, while patients could feel assured that the particular course of action that they were undertaking would in fact yield their desired outcomes. While the goal for clinical certainty in the care of individual patients is a laudable one, it is apparent that it currently remains beyond our reach and may also remain elusive. However, it has been suggested that what is keeping us from achieving this worthy goal is incomplete knowledge about the biologic and behavioral factors that are responsible for periodontal disease outcomes. It could be argued that much of the impetus for basic and clinical periodontal research, and the rationale for us to understand the mechanisms of disease in more detail, derive from the desire to identify, develop and implement more effective and predictable interventions. Thus, the more fully one can understand risk factors and accurately identify and quantify them in patients, the more accurately one may be able to predict patient outcomes.

As Nunn (28) has stated, 'with the large array of factors that influence the development and progression of periodontitis, understanding what the relationships of these various factors and determinants are to the initiation and progression of periodontal disease can be daunting.' In addition, it remains unclear what the best means are by which to combine multiple factors to yield the best estimation of prognosis. However, periodontics is not alone in this issue, as clinicians and researchers working in other

chronic, multifactorial diseases, such as cardiovascular disease, are facing similar challenges.

It has also been recognized that risk-assessment tools based on a combination of multiple risk factors, such as the Framingham Risk Score for cardiovascular disease, have important 'limitations when applied to clinical practice – performing reasonably well for groups but not necessarily for individuals' (6). Moreover, while there is great interest in the role of biomarkers, including genetic factors, in improving risk prediction for cardiovascular disease, there remain important 'questions of how much incremental value is provided and what the best metrics are to quantify improvements in screening performance' (6). Thus, the field of periodontics may take some comfort in the observation that 'despite decades of research and the introduction of numerous candidate biomarkers and putative risk factors, risk prediction for cardiovascular disease...appears to have progressed only marginally' (6). As Jackson & Wells have aptly noted (20), 'prediction is difficult, particularly about the future.'

Periodontal risk assessment, screening tools and risk calculators

Risk assessment is an accepted component of the American Academy of Periodontology guidelines for patient management (1), which state that it 'should be part of every comprehensive dental and periodontal evaluation.' The recent American Academy of Periodontology Statement on Risk Assessment (2) also notes that 'risk assessment goes beyond the identification of the existence of disease and severity, and considers factors that may influence future disease progression. ... Identifying adverse changes in risk factors, which might be suggestive of disease onset or progression (defined as deteriorating risk profile), is an important clinical concept.' It thus appears that clinicians are being encouraged to incorporate into their practice routine the belief that the more that is known about the patient's biology and behaviors (i.e. the patient's risk factors) the better that one can predict the outcomes of care. In fact, a key premise for the promotion of various periodontal diagnostic tests and of the PreViser RiskCalculator™ (31, 32, 41) has been that the identification of specific risk factors in a given patient is valuable for predicting that patient's clinical outcomes.

A distinctly different goal of risk assessment is to identify individuals who are likely, or at least more likely than others, to have periodontitis in settings

where a clinical dental examination is not available. Such a tool may be useful for screening purposes (e.g. as applied by physicians and other nondental care providers in order to assess whether referral of a patient to a dentist or periodontist is warranted), disease surveillance (e.g. as part of large telephone surveys such as the U.S. Centers for Disease Control's Behavioral Risk Factor Surveillance System), or for applications in large epidemiologic studies where a clinical dental examination on all subjects may not be feasible or may be too costly.

The American Academy of Periodontology has developed its own proprietary risk calculator and has made it freely available on its website as a 'self-assessment tool' in order to provide a public service (3). The web-based tool of the American Academy of Periodontology is easy to use and is in part based on the premise of the accuracy of patient self-reports regarding signs and symptoms of periodontitis as well as their having certain periodontal risk factors. While some may question the ability of the public and patients to recall prior diagnoses or to self-identify various health conditions, there does exist an extensive literature indicating that patient self-reports can be useful for specific applications (4, 9, 14, 34, 40).

A recent systematic review (4) found that one good self-report measure was actually the simple question, 'Has any dentist/hygienist told you that you have deep pockets?', which had a sensitivity of 55%, a specificity of 90%, a positive predictive value of 77% and a negative predictive value of 75%, which were all calculated using actual clinical pocket depth as measured by clinicians. The systematic review further suggested that 'higher validity could potentially be obtained by the use of combinations of several self-reported questions and other predictors of periodontal disease.'

The data supporting the accuracy of self-reports has come from both population-based epidemiologic studies as well as from clinical practice-based patient samples. Recently, Dietrich et al. (9) showed that depending on the definition used for their study's gold-standard periodontal disease, only two self-reported periodontal status items (in combination with age, gender and smoking status) were needed to yield an optimal predictive model fit. These items were self-reported tooth mobility and self-reported professionally diagnosed bone loss. Self-reported tooth mobility was associated strongly with periodontal disease, independently of other risk factors, and was selected in all models. For dichotomous definitions of periodontal disease, the discrimination of predictive logistic regression models was good, with areas under

the receiver operating characteristic curve being >0.80 . Assessment of periodontal disease history based on the highest and lowest quartiles of model-predicted values was found to yield high sensitivity and specificity. The authors concluded that logistic regression models which included age, gender, smoking and these two self-reported variables (i.e. mobility and professionally diagnosed bone loss), consistently yielded an area under the receiver operating characteristic curve of >0.80 for several definitions of periodontal disease. Importantly, such a receiver operating characteristic curve value has been considered to be 'excellent' (19) or 'useful' (39) in diagnosis and prognosis.

Use of periodontal risk factors in screening and prognosis: the American Academy of Periodontology self-assessment tool

The web-based self-assessment tool available on the American Academy of Periodontology website (3) is a good example of the value and limitations of how knowledge about the role of individual periodontal risk factors may be used in combination to educate patients, raise awareness and assist in decision-making. The tool's web interface is a brief 13-item questionnaire (see Fig. 1) that asks straightforward questions that most persons would be able to answer easily. The items include the person's age (three response options: <40 ; $40-65$; >65 years), and their flossing behavior (daily; weekly; seldom). Other items have simple response choices of yes or no, whereas several items in addition to the yes/no option also include the option of 'don't know' ('any of your family members had gum disease'; 'are your teeth loose'; 'do you currently have any of the following health conditions i.e. Heart disease, osteoporosis, osteopenia, high stress, or diabetes') or the option of 'don't remember' ('seen a dentist in the last 2 years'; 'ever been told that you have gum problems, gum infection or gum inflammation'). The answers to the questions are combined (using a proprietary algorithm whose details are not publicly available) to yield one of three risk categories: low risk, medium risk, or high risk.

The website informs users that by using the answers to the questions, the self-assessment tool 'will help you see if you are at risk for having or developing periodontal (gum) disease. Millions of people don't know they have this serious infection that can lead to

tooth loss if not treated. Once your answers are submitted, a proprietary calculation determines whether you are at low, medium or high risk and generates a report of your results.' Importantly, it also informs users that the tool is not 'a substitute for a comprehensive evaluation and diagnosis by a qualified practitioner. Rather, this report is intended to help educate patients about common risk factors related to periodontal diseases and to assist in the decision of when referral to a periodontist would be advisable.' An important point to note about the tool's stated aim is the singling out of tooth loss as an outcome of interest to the patient: 'this serious infection that can lead to tooth loss if not treated'.

It is important to note that in this case the self-assessment tool is being used for an educational purpose, directed primarily at those persons who may not be under the usual care of a dentist, as well as to serve the broader purpose of population-based screening. It is not being presented as a tool whose algorithm seeks to yield a high receiver operating characteristic curve value. Given its aim, one would expect that the algorithm's diagnostic sensitivity has been prioritized over its diagnostic specificity. In other words, the algorithm has probably been created to minimize the false negatives while accepting the likelihood of many false positives (i.e. in order to avoid misclassifying as low risk those persons who are truly at higher risk for periodontal disease).

This aspect of the self-assessment tool is reflected in part by the various combinations of responses that consistently yield a calculation of 'high' risk despite many or all other responses being favorable. For example, the responses shown in Fig. 1 yielded just such a result. The 'yes' answer to the question of 'Have your gums receded, or do your teeth look longer?' was sufficient to yield a 'high' risk categorization. This 'high' risk was assigned irrespective of the age group used and despite the fact that all the other answers given were favorable ones, including no mobility, no bleeding, no smoking and daily use of floss. Using other variations in the response categories can also result in a 'high' risk label, even when only one of the responses appears unfavorable and all the other responses appear favorable. However, this is not at all an unreasonable approach for a self-assessment tool intended to serve as a simple-to-use, population-based screening test.

Given the proprietary nature of the American Academy of Periodontology self-assessment tool's algorithm, it is not possible to evaluate its test characteristics in any great detail. Nevertheless, it is possible that the algorithm could be readily modified

Answer these questions to assess your gum disease risk

How old are you?

Are you female or male?

Do your gums ever bleed?

Are your teeth loose?

Have your gums receded, or do your teeth look longer?

Do you smoke or use tobacco products?

Have you seen a dentist in the last two years?

How often do you floss?

Do you currently have any of the following health conditions?
i.e. heart disease, osteoporosis, osteopenia, high stress, or diabetes

Have you ever been told that you have gum problems, gum infection or gum inflammation?

Have you had any adult teeth extracted?

Have any of your family members had gum disease?

Fig. 1. American Academy of Periodontology self-assessment tool.

to create one that would be more suitable for use in clinical practice and aid in patient education and perhaps in individual patient-level decision-making. Moreover, by incorporating various clinical and biological measures into an assessment tool, in addition to the self-report items it now contains, one could enhance its value in patient education in the clinical practice setting.

Using a similar approach, a simple set of patient characteristics and risk factors may be used to calculate the risk for heart disease and heart attack (Fig. 2). Based on the results of the Framingham Heart Study (12), a variety of cardiovascular disease

calculators have been developed. These can be as simple as the one used by the National Cholesterol Education Program (27), as shown in Fig. 2, which relies on only seven variables (age, gender, smoking, total and high-density lipoprotein cholesterol, systolic blood pressure, and current use of medication to treat high blood pressure) to calculate an individual's risk of having a heart attack over a 10-year period. Similar 'Framingham' calculators are also available for a number of other cardiovascular outcomes, such as coronary heart disease, stroke and intermittent claudication, as well as for different time horizons (12).

The risk assessment tool below uses information from the Framingham Heart Study to predict a person's chance of having a heart attack in the next 10 years. This tool is designed for adults aged 20 and older who do not have heart disease or diabetes. To find your risk score, enter your information in the calculator below.

Age: years

Gender: Female Male

Total cholesterol: mg/dl

HDL cholesterol: mg/dl

Smoker: No Yes

Systolic Blood Pressure: mm/Hg

Are you currently on any medication to treat high blood pressure. No Yes

Total cholesterol – Total cholesterol is the sum of all the cholesterol in your blood. The higher your total cholesterol, the greater your risk for heart disease. Here are the total values that matter to you:

Less than 200 mg/dl 'Desirable' level that puts you at lower risk for heart disease. A cholesterol level of 200 mg/dl or greater increases your risk.

200 to 239 mg/dl 'Borderline-high.'

240 mg/dl and above 'High' blood cholesterol. A person with this level has more than twice the risk of heart disease compared to someone whose cholesterol is below 200 mg/dl.

HDL cholesterol – High density lipoproteins (HDL) is the 'good' cholesterol. HDL carry cholesterol in the blood from other parts of the body back to the liver, which leads to its removal from the body. So HDL help keep cholesterol from building up in the walls of the arteries.

Here are the HDL-cholesterol levels that matter to you:

less than 40 mg/dl: a major risk factor for heart disease;

40 to 59 mg/dl: the higher your HDL, the better;

60 mg/dl and above: an HDL of 60 mg/dL and above is considered protective against heart disease.

Smoker – Select "yes" if you have smoked any cigarettes in the past month.

Systolic blood pressure – Systolic blood pressure is the first number of your blood pressure reading. For example, if your reading is 120/80 (120 over 80), your systolic blood pressure is 120.

Fig. 2. Risk assessment tool for estimating 10-year risk of having a heart attack.

While the Framingham cohort is suburban and primarily White, the major cardiovascular risk factors identified by the study over the past several decades have been shown to apply in other populations, although relative contributions of the variables may vary across cohorts. It is thus important that caution is used when applying an algorithm developed in one cohort to another. For example, Brindle et al. (5) examined the predictive accuracy of the Framingham risk score for coronary heart disease in a representative British population of 6643 men aged 40–59 years, who were free from cardiovascular disease at entry into the British regional heart study. They compared the observed 10-year coronary heart disease mortality and event rates for each individual with the rates predicted by the Framingham risk algorithm. They found that a nonfatal coronary heart

disease event actually occurred in 10.2% of the men as compared with the 16.0% predicted rate. This represented a relative overestimation of 57% ($P < 0.0001$). They concluded that the recommended risk scoring methods derived from the Framingham study significantly overestimated the absolute coronary risk assigned to a representative sample of individuals in the United Kingdom.

Use of periodontal risk factors in screening and prognosis: the PreViser RiskCalculatorTM

The PreViser RiskCalculatorTM, as developed by Page and colleagues (31, 32, 41), shares some characteristics with the American Academy of Periodontology

tool described above but also differs from it in several important ways. The calculator makes use of algorithms to combine, mathematically, various patient characteristics and multiple risk factors. It also yields a simple result whereby an individual patient is assigned an ordinal risk score from 1 (low risk) to 5 (high risk) in the case of the risk calculator, as compared with the American Academy of Periodontology tool that yields three categories of low, medium or high risk. In addition to including a patient's self-report information, such as that obtained in a routine health history (e.g. diabetes and/or smoking), the risk calculator also includes information regarding various clinical and radiographic findings as would be documented in a standard patient examination.

Thus, in contrast to the American Academy of Periodontology self-assessment tool, the PreViser RiskCalculator™ has been specifically designed to be used in a clinical care setting following clinical data collection. Importantly, its aim is not for broad population-based screening but rather it aims to serve the needs of a patient's own individual situation and decision-making. As described by the PreViser Corporation (35), the calculator is intended to give the clinician 'an easy to use, objective and reproducible way to measure, understand, and communicate your patients' risk and disease level as simple numeric scores.' It may also be used 'to track changes in risk level and disease severity over time to evaluate treatment effectiveness and outcomes...' and to 'differentiate between patients with the same current health/disease state, but who are at varying potentials that this state will deteriorate.'

However, as is the case with the American Academy of Periodontology tool, complete details about the risk calculator's algorithms have not been published in the peer-reviewed literature, nor has its longer-term prognostic value in a clinical care setting been systematically validated. It has therefore been difficult to evaluate the risk calculator critically and it has been referred to by Gansky (13) as a 'black box'. However, despite this limitation, it has received favorable assessments from experts in the field (7, 10) and has been validated using at least one population-based cohort study (32). Moreover, the calculator's basic characteristics have been described in some detail. Page et al. (32) reported that the 'calculation of risk is a multistep process involving mathematical algorithms that use nine risk factors, including: patient age; smoking history; diagnosis of diabetes; history of periodontal surgery;

pocket depth; furcation involvements; restorations or calculus below the gingival margin; radiographic bone height; vertical bone lesions. A 3-point scale is used to document pocket depth and radiographic bone height. An algorithm was developed to quantify disease severity from pocket depth and bone height values. The base risk score is calculated using an algorithm that correlates disease severity with age. The risk score is increased if there is a positive history of periodontal surgery and if the patient smokes more than 10 cigarettes per day, or the patient has diabetes that is poorly controlled. The existence of furcation involvements, vertical bone lesions, or subgingival restorations or calculus increase risk when the risk score is otherwise less than 4.'

As is apparent from this brief description, the risk calculator is quite complex. Moreover, it also appears that it has been constructed to be automatically self-modifying and to 'learn' from clinical experience as more patients are entered into the system and as they are treated and followed over time. One of the patients (41) related to the risk calculator and its various applications provides the following information on this novel aspect. The system first inputs diagnostic data from the healthcare provider and 'uses a subset of the diagnostic data to compute a patient's risk value by considering the sum of three components of risk, including (i) systemic risk, (ii) exposure risk, and (iii) experience risk. The subset of data used to compute risk includes the data determined by scientific analysis to be relevant in assessing a person's risk of contracting a disease, or being responsive to treatment.'

Furthermore, the 'system periodically adjusts, or updates computed risk values to increase the accuracy of the system's computation of risk values. Risk values are updated by the system for each set of 300 patients. Thus, after performing outcomes assessment, the healthcare system determines whether the next group of 300 patients, regardless of provider, has been analysed by the system (step 214). If not, processing continues to step 202. Otherwise, the healthcare system uses the patient outcomes assessment information to automatically update (i.e. adjust) the risk value computed during risk assessment (step 216). The risk update process recalculates a computed risk value. The risk update process recalculates each patient's computed value of risk to make it consistent with both the actual risk for all patients, based on values derived from the patient and provider outcomes assessment, and the patient's risk as determined by outcomes associated with previous

treatment received by that patient. This recalculation considers the value of risk-adjustment factors that represent trends in risk values among all patients. ... This risk adjustment represents one way the health-care system evolves over time. For example, during the lifetime of a patient, the patient's risk value changes due to changes in both, e.g. the patient's diagnostic information and changes in the risk update factors. By updating the risk value for each patient each time an additional 300 patients receive treatment plans approved by the system, the system increases the accuracy of both the risk-update factors and the overall computation of a risk value.'

As noted earlier, the risk calculator was validated using retrospective data from a longitudinal cohort study of adult men who had been followed for at least 15 years (32). The clinical records and radiographs of 523 subjects enrolled in the Veterans Affairs (VA) Dental Longitudinal Study and its medical counterpart, the VA Normative Aging Study, were used in the validation study. The study subjects were seen every 3 years for a complete battery of medical and dental assessments. Importantly, the men were not VA patients, but rather received both their medical and dental care in the private sector. In addition, over the first 15 years of the study few, if any, men received surgical periodontal treatment and none were included in the analyses. The cohort thus reflected the 15-year outcomes of prognoses made from baseline data without intervening definitive periodontal care.

Information from the study's baseline examination was used to create individual risk scores for subjects. These baseline data were entered into the risk calculator and a risk score on an ordinal scale of 1 to 5 was calculated for each subject. Periodontal status was determined in terms of radiographic alveolar bone loss, and tooth loss was determined from the clinical records. These outcomes were assessed at years 3, 9 and 15. It was found that the calculated risk scores were strong predictors of future periodontal status, measured as worsening severity and extent of alveolar bone loss and tooth loss, especially loss of periodontally affected teeth.

Over the entire 15-year follow-up period, the risk scores (calculated using the baseline data) consistently ranked groups from least to most bone loss and tooth loss. The risk groups differed greatly from one another. For example, by year 3 the incidence rate of bone loss of group 5 (the highest risk) was 3.7-fold greater than for group 2. Furthermore, by year 15 the loss of periodontally affected teeth was 22.7-fold

greater in group 5 than in group 2 ($P < 0.001$), while 83.7% of subjects in risk group 5 had lost one or more periodontally affected teeth compared with 20.2% of subjects in group 2. The risk categories were thus also useful in regards to predicting likelihood of tooth loss. A person's relative risk of tooth loss increased significantly in correspondence with their risk category. It was concluded that the scores generated by the risk calculator, using the type of information collected during standard clinical examinations, could 'predict future periodontal status with a high level of accuracy and validity' (32).

However, it is important to emphasize that the prognostic value shown by the use of the risk calculator in this particular study cohort was in the absence of definitive periodontal treatment over the follow-up period and with the assumption that the individual's risk score, calculated using baseline values, did not change over the follow-up period. In addition, the generalizability of the findings (derived from a relatively small cohort of predominantly White, male, veterans living in the Greater Boston area) to other populations remains uncertain. Lastly, while it is clear that the risk calculator has been designed specifically to take into account the effects of treatment and changes in risk profiles, there has as yet been no published validation of its use in that context in a large-scale clinical study.

Periodontal risk calculation: applications and limitations

The American Academy of Periodontology web-based self-assessment tool clearly illustrates the value of a risk calculator as a means by which to raise public awareness and to screen for treatment needs. The ability to combine, mathematically, multiple characteristics of a patient and to assign a single global risk score is the basic premise of the American Academy of Periodontology tool, as it is with the Framingham Heart Study cardiovascular disease risk calculators that are used for heart disease and stroke. Similarly, at the level of the individual clinician-patient interaction, it is readily apparent how deriving a summary risk score could facilitate discussion and inform decision-making about risk reduction and treatment options. But, beyond their value in patient education, is it clear that risk calculators can truly aid clinicians in making better diagnoses and prognoses? Is a computer-aided mathematical tool, such as the PreViser RiskCalculatorTM, able to yield a better diagnostic result than the typical clinician's 'gestalt'

approach? Interestingly, there is some evidence that this may be the case.

Persson et al. (33) compared the ability of a group of expert periodontists and general practitioners to assign risk scores to 107 patients based on the same set of clinical and risk factor information as was used for input into the risk calculator. They found great heterogeneity in the risk scores assigned by the clinicians, as well as an apparent underestimation of risk with fewer persons placed in the highest risk category, compared with the results produced using the risk calculator.

While it was evident from these results that even expert clinicians varied greatly in their evaluation of risk, it would be incorrect to say that the clinician's approach was wholly 'subjective.' The clinicians used the same 'objective' data as used by the risk calculator. Rather, and not surprisingly, it seems that the way that clinicians combined the multiple objective factors in order to derive a summary risk score involved more than a mathematical calculation. But, although imprecise, were the clinicians' results incorrect in any consequential manner? While the study did show great variability and apparent underestimation of risk, it was not determined whether this would in fact have resulted in any detrimental effect on patient outcomes. That is, would the clinicians' underestimation of risk, or overestimation, have led to significantly different treatment recommendations or patient outcomes? While it is a plausible assumption, it has not yet been scientifically demonstrated that the application of a periodontal risk calculator to routine patient care is actually associated with better patient outcomes. Similarly, there is a paucity of evidence showing that the use of such tools will lead to 'reduction in the need for complex periodontal therapy, reduction in oral health care costs, and improved clinician productivity and income' (30) despite the claims being made for their use.

Although presently lacking such evidence, the use of risk calculators holds much promise in clinical practice. As discussed earlier, at minimum they are already useful in promoting patient education. But they may also serve an equally important role in promoting clinician education. As Glick (15) has pointed out, there is a need to educate 'oral health care professionals regarding how to analyze risk assessment and how to translate that assessment into clinical care for individual patients'. The effort to incorporate a risk calculator in a clinical practice may lead to both better-informed patients and better-informed dental care providers. In addition to the risk

calculator component, the PreViser Oral Health Information Suite (30, 35) also provides the clinician with a set of treatment options, from a 'best practices' database, tailored to the individual patient's current calculated risk and disease state, and an outcomes assessment module that compares the effect of treatments on risk and disease states for the individual patient. Examples of the analytic reports generated may be seen on the PreViser website (35). While such a comprehensive and systematic approach to clinical decision-making would be an improvement over much current practice, additional research is needed to determine whether such tools will actually result in better patient outcomes.

In addition to the further refinement of person-level prognostic tools, research is also being conducted on the development of tooth-level risk calculators. For example, Nunn has applied a novel statistical approach that utilizes an extended form of Classification and Regression Trees for survival (11, 29, 37, 38), which compensates for multiple outcomes within an individual subject (i.e. multiple tooth loss within a person) in order to develop and test global prognostic indicators that are based on a hard outcome, namely tooth loss. Tree-based methods have attracted interest in a wide variety of fields because they require few statistical assumptions, handle various data structures readily and provide for meaningful interpretation. The need to develop meaningful assignment of prognosis in medical research has led to the generalization of regression trees to survival analysis. Because survival analysis involves actual failure times in addition to failure status, the use of regression trees with survival analysis enables one to extract more information from data compared with other analytical techniques, such as logistic regression.

Nunn et al. (29) have already applied Classification and Regression Trees for survival to the analysis of longitudinal data from a periodontal clinical practice sample to develop tooth-level periodontal prognosis based on the probability of tooth survival (Table 1). Although the classifications derived were able to relate increasing tooth loss with a poorer prognostic category, optimal results were not achieved because the prognostic categories for 'Questionable' and 'Hopeless' still had relatively high tooth survival. Part of the reason for this result may be the fact that all patients in this study were very well-maintained periodontal patients who were receiving optimal care throughout the follow-up.

Multivariate exponential Classification and Regression Trees for survival was also applied to the

Table 1. Multivariate goodness-of-split classification and regression trees for survival applied to tooth loss from periodontal disease

Group	Definition	Teeth	No. lost	Per cent lost
I	Good	454	0	0.0
II	Fair	749	9	1.2
III	Poor	1070	58	5.4
IV	Questionable	81	17	21.0
V	Hopeless	157	48	30.6

Accuracy of prediction model (prognostic groups: I = 'Good', II = 'Fair', III = 'Poor', IV = 'Questionable', and V = 'Hopeless').

N.B. Multivariate goodness-of-split Classification and Regression Trees were applied to detailed clinical data from 100 patients enrolled in previous studies of periodontal prognostic indicators conducted by McGuire & Nunn (23, 24). Although the classifications provided increasing tooth loss with a poorer prognosis, optimal results were not achieved because categories for 'Questionable' and 'Hopeless' still had a relatively high tooth survival. Part of the reason for this may be a result of the fact that all patients in this study were very well-maintained periodontal patients who were receiving optimal care throughout the follow-up.

Baseline measures of probing depth, furcation involvement, mobility and per cent bone loss were all associated with tooth loss from periodontal disease, based on the multivariate goodness-of-split tree with bootstrap pruning employed. Additionally, age, crown-to-root ratio and fixed abutment status were also associated with tooth loss from periodontal disease.

VA Dental Longitudinal Study data set to develop tooth-level global dental prognosis based on the probability of tooth survival (M.E. Nunn, unpublished results; Table 2) with promising results, although the classifications for 'Questionable' and 'Hopeless' also had relatively high tooth survival

Table 2. Multivariate exponential classification and regression trees for survival applied to the VA Dental Longitudinal Study

Group	Definition	Teeth	No. lost	Per cent lost
I	Good	934	1	0.1
II	Fair	949	47	5.0
III	Poor	1126	137	12.2
IV	Questionable	2464	533	21.6
V	Hopeless	990	385	38.9

Accuracy of prediction model (prognostic groups: I = 'Good', II = 'Fair', III = 'Poor', IV = 'Questionable', and V = 'Hopeless').

N.B. We applied the multivariate extension of the exponential hazard frailty approach to Classification and Regression Trees for survival to data from the VA Dental Longitudinal Study. We compiled a subset of 6463 teeth from 355 subjects that had complete baseline information. Among them, 1103 (17.1%) teeth were lost at some point during the 30-year follow-up. The 19 baseline factors considered for inclusion in the survival tree were as follows: tooth type (molar, premolar, cuspid, incisor), total number of teeth present, patient age, smoking status, educational level, socioeconomic level, number of endodontically treated teeth, subject-level average bone height (mm), subject-level average Schei bone loss score, tooth-level plaque score, tooth-level mobility score, tooth-level calculus score, tooth-level gingival score, maximum tooth-level Schei bone loss score, maximum tooth-level probing depth, tooth-level Decayed-Missing-Filled score (i.e. number of decayed, missing or filled surfaces), maximum decay, tooth-level endodontic treatment and tooth-level bone height (%).

Although the classifications provided increasing tooth loss with a poorer prognosis, optimal results were still not achieved.

Table 3. Multivariate exponential classification and regression trees for survival applied to the VA Dental Longitudinal Study with genetic factors included

Group	Definition	Teeth	No. lost	Per cent lost
I	Good	136	0	0.0
II	Fair	689	11	1.6
III	Poor	409	55	13.4
IV	Questionable	369	99	26.8
V	Hopeless	266	141	52.0

Accuracy of prediction model (prognostic groups: I='Good', II='Fair', III='Poor', IV='Questionable', and V='Hopeless').

(probability of tooth loss: 21.6% and 38.9% for 'Questionable' and 'Hopeless', respectively, Table 2) for such a long period of follow-up. Multivariate exponential Classification and Regression Trees was also applied to a subset of subjects in the VA Dental Longitudinal Study who also had results from testing genetic risk factors for periodontal disease with genotype included in the modeling (unpublished results; Table 3). Results for the subset with genetic information yielded better prediction, although the categories for 'Questionable' and 'Hopeless' still had a higher survival than one would expect if we are to keep such labels for prediction in the future (probability of tooth loss: 26.8% and 52.0% for 'Questionable' and 'Hopeless', respectively, Table 3).

It is worth noting that tooth type appears to be a major factor in predicting tooth loss, which indicates to us that future work in this area should include stratification by tooth type. Also, for the survival trees whose predictability are shown in Tables 1 and 2, the first cuts of those trees were root furcation (0 vs. 1,2,3) and tooth type (molar vs. nonmolar). Because these are two different sets of patients yielding similar information about the importance of tooth type in predicting tooth loss, future research must take this into account if we are to build a reasonably predictive model for assessing the prognosis of a tooth. Further research is ongoing in this area, which includes stratification by tooth type, use of random forests extended for correlated outcomes (e.g. tooth loss), and Bayesian survival trees extended for correlated outcomes. From applying random forests to the VA Dental Longitudinal Study, the variables that were found to be the most important in predicting tooth loss were: subject-level mean alveolar bone loss score at baseline, tooth-level decayed, missing or filled score at baseline and tooth type (molar, premolar, cuspid, incisor).

Conclusions

It is clear that the identification of periodontal risk factors (i.e. environmental or host factors that increase the susceptibility to periodontitis and the progression of periodontitis or that increase the likelihood of treatment failures) has contributed vastly to our understanding of the pathogenesis of periodontitis, thereby opening promising new avenues for periodontal therapy as well as for periodontal disease prevention. However, the utility of such risk factors to predict disease incidence, progression and treatment outcomes at an individual patient level remains extremely limited. This is true even for relatively strong risk factors, such as smoking, as the following example may serve to illustrate.

In order to see how a risk factor may perform poorly in discriminating disease outcomes in individuals, let us take a hypothetical population of 200 individuals, 20 of whom develop some periodontal disease end point of interest over a defined period of time (e.g. progression of periodontitis over 2 years). Smoking is a highly prevalent and arguably the strongest known environmental risk factor for periodontitis, and in our hypothetical example we assume that one out of four patients in our population is a smoker (smoking prevalence 25%). The data under analysis may be summarized in a 2×2 table (Table 4).

In this example, the relative risk for disease progression comparing smokers with nonsmokers is $(10/50)/(10/150) = 3$ (i.e. smokers are three times more likely to have progression of periodontitis). This is consistent with the strengths of association between smoking and periodontal risk that are widely reported in the literature. In epidemiologic terms, this may be considered a moderately strong association. However, the relative risk is not an appropriate measure to tell us how much better we are able to predict disease progression if we know a particular patient's smoking status. In contrast, measures of diagnostic accuracy such as sensitivity,

specificity, and positive and negative predictive values, will do so.

From the data in Table 4, we can calculate that knowing a patient's smoking status has 50% sensitivity (10 out of 20 individuals with disease progression are smokers) and 78% specificity (140 out of 180 individuals without disease progression are nonsmokers). What can we learn about a particular patient's risk of disease progression by knowing his or her smoking status? From the hypothetical data, if the risk of disease progression is 10% (20/200), our knowing that a particular patient is a smoker increases that risk to 20% (10/50). In other words, while we were 90% certain that a patient's disease would not progress before we knew anything about his or her smoking status, knowing that he or she is a smoker we are now 80% certain that the patient's disease will not progress. If our patient was a nonsmoker, we would be 93% certain that the disease would not progress.

It is thus evident from the above example that even with a relatively strong risk factor such as smoking, knowing whether or not a particular patient is exposed to a particular risk factor effectively results in only relatively minor changes in our ability to predict this patient's clinical outcome. Despite these limitations, risk calculation based on the use of one or several risk factors may increase individual patient knowledge and effectiveness of care under certain circumstances. For example, Grover et al. (18) recently showed in a randomized trial that increasing patient knowledge of their coronary risk profiles led to improved effectiveness of dyslipidemia therapy.

Thus, despite the expected future progress in the development of better prognostic indicators, it is important to remember that when we come to apply such tools to the care of the individual patient, the best we can achieve are only marginally improved estimates and not clinical certainty. As Benjamin Franklin is reputed to have observed, 'in the world nothing can be said to be certain except death and taxes.' Perhaps the lasting value of the development and broader use of risk calculators in practice will be the tacit understanding, by both patients and clinicians, that all prognoses are only probabilistic in nature.

Table 4. Association between smoking and disease progression in a hypothetical sample of 200 individuals

	Smoker	Nonsmoker	Total
Disease progression	10	10	20
No disease progression	40	140	180
Total	50	150	200

Acknowledgments

This work was supported in part by NIH grants K24 DE000419, U54 DE014264, U54 DE019275 and R21 AT003714 to Dr Garcia; R03 DE015426 and R03

DE016924 to Dr Nunn; and R03 DE016357 and R03 DE017948 to Dr Dietrich. None of the authors currently have, or have had previously, any financial interests in the development or commercialization of risk calculators.

References

- American Academy of Periodontology. Guidelines for the management of patients with periodontal diseases. *J Periodontol* 2006; **77**: 1607–1611.
- American Academy of Periodontology. Statement on Risk Assessment. *J Periodontol* 2008; **79**: 202.
- American Academy of Periodontology. perio.org 2008 Available at <http://www.perio.org/consumer/4a.html> (accessed 5/12/2008).
- Blicher B, Joshipura K, Eke P. Validation of self-reported periodontal disease: a systematic review. *J Dent Res* 2005; **84**: 881–890.
- Brindle P, Emberson J, Lampe F, Walker M, Whincup P, Fahey T, Ebrahim S. Predictive accuracy of the Framingham coronary risk score in British men: prospective cohort study. *BMJ* 2003; **327**: 1267–1272.
- De Lemos JA, Lloyd-Jones DM. Multiple biomarker panels for cardiovascular risk assessment. *N Engl J Med* 2008; **358**: 2172–2174.
- Chapple ILC. Management of periodontal diseases within the NHS three years on: are things any better? *Br Dent J* 2007; **202**: 569–570.
- Dietrich T, Garcia RI. Associations between periodontal disease and systemic disease: evaluating strength of the evidence. *J Periodontol* 2005; **76**(11 Suppl.): 2175–2184.
- Dietrich T, Stosch U, Dietrich D, Kaiser W, Bernimoulin J-P, Joshipura K. Prediction of periodontal disease from multiple self-reported items in a German practice-based sample. *J Periodontol* 2007; **78**: 1421–1428.
- Douglass CW. Risk assessment and management of periodontal disease. *J Am Dent Assoc* 2006; **137**: 27S–32S.
- Fan JJ, Su XG, Levine RA, Nunn ME, LeBlanc M. Trees for correlated survival data by goodness of split with applications to tooth prognosis. *J Am Stat Assoc* 2006; **101**: 959–967.
- Framingham Heart Study. Available at <http://www.framinghamheartstudy.org/risk/coronary.html> (accessed 5/12/2008).
- Gansky SA. Black-box periodontal risk calculator predicts alveolar bone loss and tooth loss 15 years later in a select group of nontransient men. *J Evid Based Dent Pract* 2003; **3**: 17–18.
- Genco RJ, Falkner KL, Grossi S, Dunford R, Trevisan M. Validity of self-reported measures for surveillance of periodontal disease in two western New York population-based studies. *J Periodontol* 2007; **78**(7 Suppl.): 1439–1454.
- Glick M. The numbers game. *J Am Dent Assoc* 2008; **139**: 528–530.
- Greenberg RS, Daniels SR, Flanders WD, Eley JW, Boring JR III. *Medical epidemiology, 3rd Ed.* New York, NY, USA: McGraw Hill/Appleton & Lange, 2001:10–11.
- Grossi SG, Zambon JJ, Ho AW, Koch G, Dunford RG, Machtei EE, Norderyd OM, Genco RJ. Assessment of risk for periodontal disease. I. Risk indicators for attachment loss. *J Periodontol* 1994; **65**: 260–267.
- Grover SA, Lowensteyn I, Joseph L, Kaouache M, Marchand S, Coupal L, Boudreau G. Patient knowledge of coronary risk profile improves the effectiveness of dyslipidemia therapy. *Arch Intern Med* 2007; **167**: 2296–2303.
- Hosmer DW, Lemeshow S. *Applied logistic regression.* New York: Wiley, 2000:162.
- Jackson R, Wells S. Prediction is difficult, particularly about the future. *Arch Intern Med* 2007; **167**: 2286–2287.
- Machtei EE, Dunford R, Hausmann E, Grossi SG, Powell J, Cummins D, Zambon JJ, Genco RJ. Longitudinal study of prognostic factors in established periodontitis patients. *J Clin Periodontol* 1997; **24**: 102–109.
- McGuire MK, Nunn ME. Prognosis versus actual outcome II: the effectiveness of commonly taught clinical parameters in developing an accurate prognosis. *J Periodontol* 1996; **67**: 658–665.
- McGuire MK, Nunn ME. Prognosis versus actual outcome III: the effectiveness of commonly taught clinical parameters in developing an accurate prognosis. *J Periodontol* 1996; **67**: 666–674.
- McGuire MK, Nunn ME. Prognosis versus actual outcome. IV. The effectiveness of clinical parameters and IL-1 genotype in accurately predicting prognoses and tooth survival. *J Periodontol* 1999; **70**: 49–56.
- Muzzi L, Nirei M, Cattabriga M, Rotundo R, Cairo F, Pini Prato GP. The potential prognostic value of some periodontal factors for tooth loss: a retrospective multilevel analysis on periodontal patients treated and maintained over 10 years. *J Periodontol* 2006; **77**: 2084–2089.
- National Cancer Institute. *Cancer facts.* Cancer Information Service, 2003 http://cis.nci.nih.gov/fact/8_2.htm
- National Heart Lung and Blood Institute. *National Cholesterol Education Program. Risk assessment tool for estimating your 10-year risk of having a heart attack.* <http://hp2010.nhlbihin.net/atp/iii/calculator.asp>.
- Nunn ME. Understanding the etiology of periodontitis: an overview of periodontal risk factors. *Periodontol 2000* 2003; **32**: 11–23.
- Nunn ME, Fan JJ, McGuire MK. Determination of periodontal prognostic indicators based on multivariate survival trees. *J Dent Res* 2002; **81**: 2756.
- Page RC, Martin JA, Loeb CF. The Oral Health Information Suite (OHIS): its use in the management of periodontal disease. *J Dent Educ* 2005; **69**: 509–520.
- Page RC, Krall EA, Martin J, Mancl L, Garcia RI. Validity and accuracy of a risk calculator in predicting periodontal disease. *J Am Dent Assoc* 2002; **133**: 569–576.
- Page RC, Martin J, Krall EA, Mancl L, Garcia R. Longitudinal validation of a risk calculator for periodontal disease. *J Clin Periodontol* 2003; **30**: 819–827.
- Persson GR, Mancl LA, Martin J, Page RC. Assessing periodontal disease risk. A comparison of clinicians' assessment versus a computerized tool. *JADA* 2003; **134**: 575–582.
- Pitiphat W, Garcia RI, Douglass CW, Joshipura KJ. Validation of self-reported oral health measures. *J Public Health Dent* 2002; **62**: 122–128.
- PreViser Corp. *PreViser.com 2008* (<http://www.previser.com/Dentists/default.htm>)
- Rothman KJ. *Epidemiology.* New York: Oxford Univ. Press, 2002: pp. 223 (Quote: Pp. 24–25).

37. Su XG, Fan JJ. *Multivariate Survival Trees by Goodness of Split. Technical Report 367*. Davis: Department of Statistics, University of California, 2001.
38. Su XG, Fan JJ. Multivariate survival trees: a maximum likelihood approach based on frailty models. *Biometrics* 2004; **60**: 93–99.
39. Swets JA. Measuring the accuracy of diagnostic systems. *Science* 1988; **240**: 1285–1293.
40. Taylor GW, Borgnakke WS. Self-reported periodontal disease: validation in an epidemiological survey. *J Periodontol* 2007; **78**(7 Suppl.): 1407–1420.
41. US Patent and Trademark Office. US Patent No. 6,484,144. Martin et al., November 19, 2002, Available at <http://patft.uspto.gov> (accessed 5/12/08): <http://patft.uspto.gov/netacgi/nph-Parser?Sect1=PTO1&...l=50&s1=6,484,144.PN.&OS=PN/6,484,144&RS=PN/6,484,144>.
42. Van Dyke TE, Sheilesh D. Risk factors for periodontitis. *J Int Acad Periodontol* 2005; **7**: 3–7.
43. White BA, Maupome G. Making clinical decisions for dental care: concepts to consider. *Spec Care Dent* 2003; **23**: 168–172.