Session B
Periodontal Risk Management (PRM)

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The goal of periodontal therapy is to substantially lower the risk for future progression of periodontitis (Page and Beck, 1997). A literature search yielded more than 400 published articles related to periodontitis and risk assessment. Many of these published articles were primarily speculative in nature. Except for studies assessing the influence of individual periodontal risk factors at a tooth-site basis there appears to be few comprehensive studies assessing what risk factors are associated with periodontal disease at the subject level. Information on how clinicians assess periodontal risk for disease progression in the absence of care is almost non-existent. However, in one study it was concluded that there are significant disagreements between clinicians on the scale of risk assessment and that clinicians appear to predominantly base their risk assessments on radiographic evidence of bone loss, excluding most factors that have otherwise been associated with risk for future periodontal disease activity (Persson et al, 2003).

There are four terms that are needed to be familiar with in the assessment of perceived risk for disease: 'prior odds', 'posterior odds', 'test sensitivity' and 'test specificity'. If, for example, information on disease prevalence is used to assess risk, a prevalence rate of 30% would indicate that 3:10 subjects in the population would have the disease (ratio of disease frequency to non-disease frequency in the population). This equals the prior odds of disease (with no clinical information) and chance alone one would be correct three times out of ten. If a specific diagnostic test is used which yields a specific test result, i.e. 20%, then 2:10 would have the disease and the posterior odds would be 2:10 (ratio of disease frequency to no disease frequency in those with a particular test result). In order to appreciate the posterior odds it would therefore be necessary to have information about test sensitivity (test ability to correctly identify those with disease from those with no disease) and test specificity (test ability to identify those with no disease among all tested subjects) and both those functions are impacted by the prevalence of disease in the cohort of subjects studied. Most people are poor intuitive statisticians and commonly make errors in assessing risks. The Bayes' theorem* provides a mathematical formula by which both prior odds and posterior odds are considered in assessing the probability of correctly predicting disease in the patient population providing the correct likelihood ratio:

$$\frac{(\text{Test Sensitivity}) * (\text{Disease Prevalence})}{(1\text{- Test Specificity}) + (1\text{- Disease Prevalence})}$$

Periodontal risk management (PRM) is applicable both to subjects without, or with a past history of periodontitis. Successful PRM can only be achieved if accurate information about disease prevalence and appreciation of the ability of any diagnostic test to correctly identify those

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* Bayes' theorem was developed by the 18th century mathematician, The Reverend Thomas Bayes

with disease can be used. The likelihood of successful prevention of periodontitis or successful management of those who have been successfully treated with initial cause related therapy (ICRT) must significantly exceed a ratio of 1:1. One of the major problems in the diagnosis of periodontitis has been the lack of accepted diagnostic tests with known accuracy (sensitivity/specificity characteristics). There are several studies published during the 1980 s (not referenced here) suggesting that routine clinical diagnostic procedures had poor diagnostic criteria. Major efforts were initiated aiming at the development of qualitative diagnostic periodontal tests. In principle, however, there is currently no specific periodontal diagnostic test that can be recommended or has obtained approval by, i.e. FDA (The U.S. Food and Drug Administration) and commercially available.

PRM is therefore dependent on the ability of the oral healthcare provider (Periodontist, Dentist, and Dental Hygienist) to identify the patient's risk of developing caries and periodontitis in order to provide appropriate preventive or interceptive care determined on evidence-based periodontology. Any clinician is limited in his/her ability to correctly interpret clinical information and may either overemphasize the importance of positive findings or misinterpret negative findings. Observer errors can often be attributed to: 1) the ambiguity of findings such as deep probing depth but with no bleeding on probing; 2) conditions under which the observation is made such as at distal aspects of tooth surfaces; 3) the expectations the clinician may have before making an observation; and 4) the impact of peer influence (i.e. "we think it is better to provide care than to underestimate the risk of disease").

Clinical periodontal decision-making is a complex decision process involving a process different from one that is based on a single clinical observation (i.e. probing depth, or bleeding on probing alone). The use of a comprehensive risk assessment model (PRM) is therefore critical in an accurate decision making process supporting a transition from a dental repair model to a wellness model of care. The evaluation of risk factors requires that both 'within-subject' and 'between-subject' comparisons must be considered (Mancl et al, 2000).

A comprehensive model for understanding of the pathogenesis of periodontitis has been presented (Page and Kornman, 2000). This model includes: 1) the etiological role of infectious factors; 2) the regulating effects of genetic factors; 3) the cellular and humoral immune responses to challenge and triggered release of cytokines, enzymes, hormones, and other factors controlling cell functions; and 4) the extrinsic influence of social and behavioral factors. These four cornerstones serve as the background for the clinical presentation of periodontitis and have applicability to both prior and posterior risk assessments of periodontitis.

The objective of this report was to provide background evidence on factors associated with periodontitis and guidance for PRM. Thus, an online computer search was performed (Entrez-PubMed) excluding publications older than 1980. In principle, all review articles were excluded. The following search terms were used: 'periodontal risk management', 'periodontal risk assessment', 'periodontitis and diagnosis'. 'periodontitis and diagnosis and risk', 'periodontitis and gingivitis', 'periodontitis and prevalence', 'odds ratio and smoking and periodontitis', 'odds ratio and socio-economic factors and periodontitis', 'odds ratio and age and periodontitis', 'periodontitis and systemic disease', 'genetic factors and periodontitis', 'human genome and periodontitis', 'odds ratio and bacteria and periodontitis', 'host immunity and periodontitis and treatment', 'cytokines and periodontitis and treatment'. The search term 'periodontitis and prevalence' was limited to publications between 2000 and 2003. The present report is based on selected published studies in peer-reviewed periodicals from which information related to PRM could be extracted.

The report is presented in sections with the following subtitles:

1. The role of information on the prevalence of periodontitis in PRM
2. The role of information on the presence or absence of pathogens associated with periodontitis in PRM
3. The role of genetic information in PRM
4. The role of host immunity factors in PRM
   - Cellular and humoral immunity
   - Information on the role of cytokines in assessment of susceptibility to periodontitis and value for PRM
5. The value of information about extrinsic influence of social and behavioral factors in PRM
   - Smoking as a factor
   - Socio-economic and behavioral factors, stress, and access to dental care
   - Psychological factors
6. The role of systemic diseases and periodontitis in PRM
7. The predictive value of routine clinical parameters in PRM
   - Probing depth
   - Bleeding on probing
   - Radiographic evidence of alveolar bone loss
   - Tooth loss
   - Supportive Periodontal Therapy
8. A model for PRM.

1) THE ROLE OF INFORMATION ON THE PREVALENCE OF PERIODONTITIS IN PRM

Knowledge about the prevalence of periodontitis in the patient population is necessary to develop a PRM strategy. Comprehensive documentation on the prevalence of periodontitis has been documented from the United

Table 1 Examples of the prevalence of periodontitis in different countries

Study Identification	Prevalence	Country
Albandar et al, 1999	35%	USA
Borrell et al, 2002	30%	USA
Cutress, 2001	100%	South Pacific Tokenau Island
Albandar et al, 2002	33% for men 22% for women	Uganda
Behbehani and Shah, 2002	18%	Kuwait
Sheiham and Netuveli, 2002	7% 18% 18% 30% 31%	Finland Germany Spain Russia France

States. The most recent NHANES III study (National Health and Nutrition Evaluation Survey) has demonstrated that the prevalence of periodontitis is 11.9% and with a higher prevalence of periodontitis among African-Americans. However, dependent on how periodontitis is defined the NHANES III yields different numbers on prevalence and a rate of 35% has been published (Albandar et al, 1999). After adjustment of covariates, African-Americans are 2.1 times more likely to have periodontitis than Caucasian-Americans (Borrell et al, 2002). Furthermore, comparing data from NHANES I and NHANES III this difference appears to have increased. Social, cultural and behavioral factors have, therefore, been suggested as an explanation and thereby a potential risk condition whereas minority status alone is not a significant risk condition because different ethnic minorities do not share the same health profiles (Borrell et al, 2002b). Oral health status among children in Tanzania suggests that evidence of gingivitis among 15-year-old Tanzanians was only found among 25% of them suggesting a low risk for periodontitis in this population (Kikwilu and Mandari, 2001). Other types of periodontitis, such as necrotizing gingivitis which is uncommon among otherwise healthy adolescent and adults in Northern Europe and in the United States, are much more prevalent (6.7%) in subjects between the ages of 12 and 21 years in Chile. This may suggest different patterns of disease in different regions (Lopez et al, 2002). A summary of prevalence estimations for periodontitis in different countries illustrates the inconsistency in reports on periodontitis prevalence (Table 1).

One of the major concerns about published studies on the prevalence of periodontitis is the lack of consistency in the definition of the disease as well as in the criteria for recruitment of subjects which may result in under-representation of disadvantaged groups (i.e. elderly, subjects with significant systemic disease, low income).

The lower the prevalence of a disease in a population the more difficult it would be to predict the presence of disease. Thus, the requirements on a diagnostic test will increase if it can be anticipated that only a small number of subjects in the population has the disease. Thus, with increasing disease prevalence rates the greater the likelihood of being correct in a random estimate of periodontitis risks. The lower the prevalence the greater the need for accurate diagnostic tests (high sensitivity). From a PRM perspective it is important to be aware of the prevalence of periodontitis among the pool of subjects under care of the oral healthcare provider. Data from Finland, Russia or USA would yield significantly different likelihood ratios of finding subjects at random with periodontitis. A comprehensive periodontal preventive programs such as suggested in Sweden during the 1980 s (Axelsson and Lindhe, 1981) would be of limited cost-effective value for current Finnish populations but more useful in both Russia and the United States assuming the 7% versus 30% and 35% prevalence rates are correct.

In the low risk scenario, PRM can be focused on a small target group of subjects who express a composite of conditions that have been associated with periodontitis and then be specifically targeted at addressing individual risks, i.e. through active consideration of smoking cessation. In the high risk scenario PRM could be more generalized and focused on group prevention and the use of auxiliaries in plaque control programs to prevent disease, or focus on the development of a vaccine.

In summary:
- the lower the prevalence of disease the more difficult it would be to identify subjects with disease without using accurate tests
- to be cost effective PRM would be different in low risk populations as compared to PRM in high risk populations.

2) THE ROLE OF INFORMATION ON THE PRESENCE OR ABSENCE OF PATHOGENS ASSOCIATED WITH PERIODONTITIS IN PRM

A large volume of studies has demonstrated that bacterial infection is a most significant factor in a cascade of pathogenic events resulting in clinical periodontitis. Many studies have been published on the presence of key putative pathogens associated with periodontitis. One of the problems is that it has not been possible to identify one specific pathogen that exclusively causes periodontitis. The reason for this is that periodontitis is most likely a mixed infection. Furthermore the infectious cause of periodontitis is an indigenous microflora that potentially can become pathogenic. Nevertheless characteristic patterns of a complex microflora have been identified (for review see Slots and Ting, 2002). However, many pathogens are found in periodontal pockets that have not yet been identified. Different ethnic groups may also harbor specific patterns of infections and inflammatory responses and may therefore result in ethnically specific forms of periodontitis (Holyle et al, 1990). Thus, it may be necessary to consider ethic differences in PRM strategies. For example, after adjustment for socio-demographic factors in the NHANES III study, poor periodontal status has been associated with oral *Heliobacter pylori* infection although *H.pylori* is not routinely found in periodontitis but considered as a pathogen in the gastro-intestinal tract (Dye et al, 2002). The strongest evidence for some pathogens can be sought from studies providing odds ratios for subjects with a diagnosis of periodontitis and harboring *P.gingivalis* (OR = 12.3), *A.actinomycetmecomitans, T.forsythensis* (OR = 10.4) or *M.micros* (OR = 7.7) in sub-gingival pockets (van Winkelhoff et al, 2002). Thus, if a patient carries these pathogens, such information could be considered in PRM aiming at the reduction or the eradication of such pathogens.

Studies of 7 – 12 year-old children who had limited access to dental care have been shown to have high prevalence rates of *P.gingivalis* also in other areas of the oral cavity than in periodontal sulci and pockets (Sanai et al, 2002). Furthermore antibiotic resistance to such pathogens is common although these children had not necessarily been exposed to antibiotics or periodontal therapies (Sanai et al, 2002). Even higher prevalence rates for *P.gingivalis* have been reported for children between the ages of 18 and 48 months and with a high likelihood that microorganisms are dispersed from parents to children (Tuite-McDonnell et al, 1997). From a PRM perspective, it may therefore not be sufficient to treat the affected subject but also to consider the potential risk that the subjects can be re-infected via family contacts.

Strategies for periodontal risk assessment require consideration of both the specific types and patterns of bacterial colonization and the impact of the biofilm in which these pathogens exist. Biofilms constitute a large community of different organisms in a glycocalyx providing protection and nutrition (Costerton et al, 1994). In part, the biofilm formation explains antibiotic resistance (Hoyle et al, 1990). A strategy that includes local, or systemic antibiotic administration alone, may therefore not be effective if the biofilm is not simultaneously interrupted and antibiotic therapy may only be effective with concomitant subgingival debridement.

The effects of subgingival debridement on the subgingival microflora appear to differ by species. Whereas *P.gingivalis, T.forsythensis*, and *T.denticola* are affected by subgingival debridement, such therapy does not appear effective to eradicate *A.actinomycetem-comitans* (Haffajee et al, 1997; Renvert et al, 1990). Pre-treatment presence of key pathogens may therefore predict the risk for re-infection after debridement (Shiloah et al, 1996). The likelihood of clinical attachment loss in the presence of *T.forsythensis* is high (Odds ratio 5.3, 95% CI 1.3 – 22.5, $p < 0.05$) whereas baseline information on the presence of *P.gingivalis* or *A.actinomycetemcomitans* would not yield similar predictive information (Buchmann et al, 2000). In subjects with aggressive periodontitis the odds ratio of a concurrent presence of *P.gingivalis, T.forsythensis* and *C.rectus* and evidence of periodontitis activity as defined by gingival fluid aspartate aminotransferase levels (AST test) is significant (OR = 2.2) (Kamma et al, 2001). Thus, if chance alone is 1:1 (50% chance) the likelihood of being correct in predicting disease activity knowledge of the microbiota would increase the likelihood of being correct to 2:1 (67% chance) assuming the AST test result is correct in identifying disease activity.

Studies documenting the role of bacterial information on the outcome of periodontal therapy and risk estimations are presented (Table 2). Summarized results from selected studies on ICRT and adjunct systemic antibiotics (predominantly combinations of metronidazole and amoxicillin) are presented (Table 3). Unfortunately study protocols vary greatly. Few subjects have been involved in each arm of study with varying observation periods and lack of stringency of SPT makes it difficult to interpret the results.

Antibiotic resistance among putative periodontal pathogens has been documented in several studies (i.e. Sanai et al, 2002; Winkel et al, 1998; for review see: Slots and Ting, 2000). However, antibiotic resistance may also disappear within a few months after antibiotic treatment (Ferres et al, 2002). A general concern about

Table 2 Summary of recent studies on the clinical outcome of periodontal therapies and usefulness of microbiological information. (A.a = *A.actinomycetemcomitans*, T.f = *Tannereller forsythensis*, P.g = *Porphyromonas gingivalis*, P.i = *Prevotella intermedia*, T.d = *Treponema denticola,* AP = adult periodontitis, SD = subgingival debridement, OS = osseous surgery, PD = probing depth, CAL = clinical attachment level, BOP = bleeding on probing, PCR = polymerase chain reaction, AP = aggressive periodontitis, CP = chronic periodontitis)

Study Identification	Pathogens studied/subjects	Clinical outcome and significance of microbial information
Fujise et al, 2002	P.g, T.f and A.a by PCR method 56 subjects with AP	3 months after SD sites from 56 subjects with CP. Improvement showed reduced presence of P.g and B.f (75% to 43% of sites). Non-responding sites with no change in P.g/B.f presence. No change in BOP if A.a present at baseline
Levy et al, 2002	DNA–DNA hybridization assay for 40 taxa-analysis of subgingival periodontal microflora	12 months result from 18 subjects with CP. 19 taxa significantly reduced at OS responding sites. 16 taxa significantly reduced at SD responding sites. Remark: study protocol a mixture between OS and SD in the same subject
Feres et al, 2001	DNA-DNA hybridization assay subgingival full-mouth plaque samples from all teeth in 17 subjects before and after SD and amoxicillin or metronidazole treatment	12 months results from 9 and 8 CP subjects. Total reduction of bacterial load after SD treatment. Proportions of P.g, T.f and T.d approached baseline values at 12 months. Combined treatment effective in reducing PD, CAL and BOP
DeSoete et al, 2001	DNA-DNA hybridization assay. Subgingival full-mouth plaque samples before and after one stage full mouth SD.	8 months results from 9 CP and 6 AP subjects. P.g and T.f levels at 8 months below detection level
Doungudomdacha et al, 2001	Quantitative PCR method from subgingival plaque samples	3–6 months data in 50 subjects treated with SD. P.g was reduced from 96% to 52% at sites with PD> 5 mm at baseline. A.a was reduced from 97% to 32% at sites with PD> 5 mm at baseline. P.i was reduced from 97% to 40% at sites with PD>5 mm at baseline
Sewon et al, 1999	Plaque samples from deep pockets before and after SD and periodontal surgery	Study of 29 subjects and 55 sites. Pretreatment levels of P.g., T.f and P.i had no impact on healing after treatment
Feres et al, 1999	DNA-DNA hybridization assay. Subgingival full-mouth plaque samples before and after treatments. 33 species were studied	Study of 10 test and 10 control subjects systemic doxycycline/placebo. Outcome after 90 days. Levels of P.g, T.f and A.a were not affected by treatment. Levels of 4 Actinomyces species were lowered. Levels of 3 Streptococci species were elevated after treatment.

antibiotics resistance should be considered in PRM and the use of antibiotics in the treatment of a low-grade infection should be considered calling for restrictive use. In order to reduce the risk for resistance, several studies have assessed the efficacy of local administration of antibiotics as an adjunct treatment during ICRT. Several studies have reported short-term results (less than one year) or used split mouth designs. (Garrett et al, 1999, 2000; Wennström et al, 2001; Salvi et al, 2002). One large double blinded randomized multi-center study over 12 months using site-specific administration of a slow release minocycline preparation demonstrated significantly better results at periodontal sites treated with local antibiotic as an adjunct to routine non-surgical ICRT in terms of reduction of bleeding on probing, pocket depth reduction, and resulting in gain of clinical attachment than the controls (Williams et al, 2001). However, this study did not provide evidence whether key patho-

Table 3 Select studies on the use of combined ICRT and systemic antibiotics and treatment outcomes. (A.a = A.actinomycetemcomitans, P.g = P.gingivalis, T.f = T.forsythensis, AP = aggressive periodontitis, CP = chronic periodontitis, TX = treatment, IRCT = initial cause related therapy, SPT = supportive periodontal therapy)

Study Identification	Procedures/subjects	Clinical outcome and significance of microbial information
Mombelli et al, 2002	17 subjects treated with local tetracycline fibers guided by microbiological diagnosis thereafter additional TX with amoxicillin/metronidazole for 7 days	Reduction but not elimination of A.a, P.g. Added systemic antibiotic therapy further reduced A.a and P.g. Recolonization of A.a and Pg.
Buchmann et al, 2002	13 subjects with AP given ICRT and amoxicillin + metronidazole and SPT	Successful arrest of disease in 95%. No microbiological data
Rooney et al, 2002	66 subjects with CP treated with non-surg. ICRT and with one of 4 antibiotic regimens for 7 days.	Significant improvement in subjects treated with adjunct metronidazole and amoxicillin
Feres et al, 2001	17 adults with CP treated with non-surg. ICRT + 14 days amoxicillin or metronidazole systemically	Statistically significant reduction of P.g, T.f and T.d in both amoxicillin and metronidazole treated groups. No control group
Sigusch et al, 2001	48 subjects with treated with non-surg. ICRT followed by additional ICRT and either Clindamycin, metronidazole, doxycycline or placebo and then followed for 24 months	P.g and A.a almost eliminated in clindamycin and metronidazole groups but not in the other groups. Clinical improvements best in clindamycin and metronidazole groups
Winkel et al, 2001	49 subjects with CP treated with non-surg. ICRT and either placebo or metronidazole plus amoxicillin and followed for 3 months	Reduction of deep probing depth similar, less BOP in antibiotic group, no difference in CAL change, sign. > reduction of P.g, T.f, and P micros in antibiotic group
Chavez et al, 2000	39 subjects with CP treated with non-surg. ICRT plus doxycycline 21 days followed for six months	Additional bone loss associated with presence of P.g (PPV 84%, odds ratio 31.9). No additional effect of antibiotics in bone loss
Lopez et al, 2000	46 subjects with CP treated with metronidazole and amoxicillin during one week as the sole therapy or placebo without other ICRT followed for 12 months	Significant clinical improvement in antibiotics group. Main gain in CAL 0.4 mm
Winkel et al, 1999	21 subjects with CP treated with ICRT after six weeks adjunct systemic administration of amoxicillin with clavulanic acid for 10 days	Similar clinical improvements in both groups. No difference in the microflora between test and control groups at 12 months

gens had been eliminated or not. It is obvious that the evidence-base is limited and that many studies have been performed over short time periods and that long-term results over some years would be needed for the evaluation of such adjunct antibiotic regimens. Outcomes of cost-benefit analysis from adjunct local antibiotics administrations have not been reported and are also required for proper PRM. Summarized results from studies on local antibiotics are presented in Table 4.

In summary:

- putative pathogens can be obtained in plaque samples from both apparently periodontally healthy subjects and in subjects with periodontitis
- information about the presence of pathogens associated with periodontitis at sites and in patients with periodontitis undergoing treatments may not necessarily enhance the predictability of effective PRM
- systemic administration of doxycycline does not seem to provide predictive additional benefits over ICRT alone
- ICRT and adjunct metronidazole and amoxicillin appears to have effect on microbial distribution and enhanced results in antibiotic treated groups over ICRT alone but long-term effects are unknown
- combination treatment including ICRT and amoxicillin plus metronidazole is more effective in subjects who carry *P.gingivalis, T.forsythensis*, and *A.actinomycetem-*

Table 4 Select studies on the use of combined ICRT and systemic antibiotics and treatment outcomes. (A.a = *A.actinomycetemcomitans*, P.g = *P.gingivalis*, T.f = *T.forsythensis*, AP = aggressive periodontitis, CP = chronic periodontitis, TX = treatment, IRCT = initial cause related therapy, SPT = supportive periodontal therapy)

Study Identification	Procedures/Subjects	Clinical outcome and significance of microbial information
Mombelli et al, 2002	17 subjects treated with local tetracycline fibers guided by microbiological diagnosis thereafter additional TX with amoxicillin/metronidazole for 7 days	Reduction but not elimination of A.a and P.g. Added systemic antibiotic therapy further reduced A.a and P.g. Recolonization of A.a and P.g
Williams et al, 2001	748 patients with moderate to advanced periodontitis were enrolled in a multi-center trial and randomized to 1 of 3 treatment arms: 1) scaling and root planing (SRP) alone; 2) SRP plus vehicle; or 3) SRP plus minocycline microspheres	Scaling and root planing plus minocycline microspheres is more effective than scaling and root planing alone in reducing probing depths in periodontitis patients
Puruker et al, 2001	Comparing tetracycline fiber versus systemic administration after ICRT. 15 subjects with CP in each group	Local delivery of tetracycline by a fiber or the systemic administration of amoxicillin/clavulanic acid given 3 months after scaling and root planing produced similar clinical outcomes over the 9-month observation period
Garrett et al, 2000	Comparing doxycycline by local delivery without ICRT versus ICRT in 141 subjects with CP and followed for nine months	Results show that both DH without concomitant mechanical instrumentation and SRP were equally effective as SPT in this patient group over the 9-month study period
Garrett et al, 1999	Comparing local administration of doxycyline to non-surg. ICRT in 411 subjects followed for nine months	Results of this trial demonstrate that treatment of periodontitis with sub-gingivally delivered doxycycline in a biodegradable polymer is equally effective as scaling and root planing and superior in effect to placebo control and oral hygiene in reducing the clinical signs of adult periodontitis over a 9-month period

comitans. PRM may be improved if prior knowledge of bacterial presence is accounted for and the use of appropriate combination therapy of antibiotics and ICRT but long-term effects are unknown.

- local administration of antibiotics may provide a useful approach as a component of ICRT and PRM .

3) THE ROLE OF GENETIC INFORMATION IN PRM

Many published study results on the relationship between genetic factors and periodontitis have mainly been related to family studies of specific unusual forms of periodontitis and often associated with other inherited systemic diseases. The human genome project is of such current status that newly acquired information on human genes and disease has yet to focus on the role of specific gene factors attributable to periodontitis. Studies of monozygotic and dizygotic twins have concluded that specific, unusual forms approximately 50% of all cases of periodontitis can be explained by genetic factors (Michalowicz et al, 1999). Nonetheless genetic factors and early family environment cannot explain patterns of the periodontal microflora in mono- and dizygotic twins reared together or separately (Michalowicz et al, 2000).

A genetic marker (PST) is commercially available to determine a polymorphism genotype of patients who may be more susceptible to periodontitis. Thus, subjects who are genotype positive for Interleukin- 1 gene polymorphism (IP) appear to have more advanced periodontitis than IP genotype negative patients of the same age (Kornman et al, 1997). There is also evidence that IP positive patients may be more susceptible to tooth loss than IP negative subjects (McGuuire and Nunn, 1999). Prospective studies have shown that IP positive non-smoking subjects over the age of 50 have significantly deeper periodontal pocket probing depths than their IP negative counterparts (Cullinan et al, 2001). Analysis of data from young adults has also suggested that the IL-1A(+ 4845) (1,1)/IL-1B(+ 3953) (2,2) geno-

type is associated with periodontitis (Thomson et al, 2001). The extent of bone loss at initial examination and positive Il-1 gene polymorphism test has been shown to be a robust predictor of future attachment loss in well-maintained subjects on SPT (Nieri et al, 2002). Consistent with these findings a study of Il-1 genotype positive non-smoking patients enrolled in an SPT program for several years previously had significantly higher bleeding on probing (BOP) percentages at recall visits than IP negative patients (Lang et al, 2000).

Retrospective studies on the influence of Il-1-1 genotype and periodontal status have shown that although information about Il-1-1 genotype provides a partial explanation to past history of periodontitis, such information cannot explain future alveolar bone loss in non-smokers (Cattabriga et al, 2001). Other studies confirm these conclusions that the knowledge about Il-1 1 haplotype does not provide useful information in predicting the risk for disease progression following therapy (Ehmke et al, 1999). No differences in clinical attachment loss between non-smoking Il-1 gene positive and negative subjects have been reported, while smoking and being Il-1 gene positive was associated with risk of clinical attachment loss (odds ratio: 4.2, 95% CI: 1.03 – 16.7) (Meisel et al, 2002). The cost effective value of Il-1 gene polymorphism testing has been studied by traditional decision tree analysis controlling for anticipated periodontal treatment costs demonstrating that testing for the Il-1 gene polymorphism has limited value. (Higashi et al, 2002). In part, the study used known risk data and assumptions of treatment efficacy limiting the informative value of the study. In contrast other studies have shown that baseline levels of Il-1 and Il-8 and granulocyte elastase in gingival fluid are explanatory for short-term outcome of periodontal therapy (Jin et al, 2002). Similar conclusions have also been drawn from retrospective studies of patients on SPT in that Il-1 gene positive subjects have more non-responding sites that Il-1 gene negative subjects (McGuire and Nunn, 1999).

In summary:

- genetic factors are of importance in the pathogenesis of periodontitis and may explain susceptibility
- new information on specific genetic factors may in the future be useful in PRM
- information on interleukin 1 gene polymorphism appears to be valuable in PRM.

4) THE ROLE OF HOST IMMUNITY FACTORS IN PRM

Cellular and Humoral Immunity

A large volume of studies has focused on protective and destructive aspects of both cellular and humoral immunity and on the role of cytokine expression in periodontitis. However, relatively few studies have provided information useful for PRM. Early studies on the pathogenesis of periodontitis focused on the cellular immune system and the presence of polymorphnuclear leukocytes (PMN) in inflamed gingival tissues. However, there is currently no recent data to suggest that information on the extent of PMN cell infiltration would yield valuable information in PRM.

Studies have identified that putative periodontal pathogens have the ability to modulate the immune response and bypass host defense mechanisms and either invade cells (Lamont et al, 1992), or modulate the immune response (Teng et al, 2000). In subjects who are not infected by *A.actinomycetemcomitans* the serum levels of immuno-competent cells decrease after successful non-surgical treatment, whereas *A. actinomycetemcomitans* infected subjects do not appear to experience the same reductions suggesting that *A.actinomycetemcomitans* alter the host immune response (Kleinfelder et al, 2001).

Recent evidence suggests that a combined microbial colonization/antibody response profile can effectively identify periodontitis patients (Papapanou et al, 2000). Thus, combined knowledge about characteristic microbiota and serum titers to antigens may be a useful diagnostic aid but would not necessarily enhance the ability to predict outcome or support PRM. In at least one study, patients with chronic periodontitis have shown that periodontal therapy affects the magnitude and quality of the humoral immune response to suspected pathogens, and that the effect is dependent on initial serological-status which may have a bearing on treatment outcome (Mooney et al, 1995). However, this study included only a small set of subjects with 5 months follow-up time.

Several efforts have been made towards the development of a vaccine against periodontitis. Animal studies have shown promising results and it appears that tested whole cell *P.gingivalis* vaccines, as well as purified protein and DNA vaccine may be safe to use and effective in reducing/preventing experimentally induced periodontitis in animal models; but no such vaccine studies have been performed in humans. Thus, any modulation of the host immune system by raising antibodies would currently depend on passive immunization, i.e. subgingival debridement, which results in bacteremia inducing a host response. There is no information on what antibody titer levels would provide effective humoral protection against periodontitis infection. Hence, titer values can currently not be used to predict outcome of periodontal therapy or be useful in PRM.

Information on the Role of Cytokine in Assesment of Susceptibility to Periodontitis and Value for PRM

In the previous section on the role of genetic information in PRM it is clear that interleukin 1 (Il-1) gene polymorphism has been a primary target of study. Il-1 -1 is locally produced and released in gingival fluid (Masada et al,

1990). Subjects with severe periodontitis also have significantly higher Il-1β levels in gingival fluid at shallow sites than subjects with limited periodontitis confirming a characteristics difference in Il-1 1 response (Engebretson et al, 2002). There are few studies that actually have assessed the significance of Il-1 gene status in relation to treatment outcomes and the predictive value of information of Il-1 gene haplotype status.

Levels of prostaglandin E2 (PGE_2) in gingival fluid have also been studied to assess the value of information on PGE_2 as a predictive marker of treatment outcome. However, limited studies are available for review. Although studies have shown that PGE_2 can be associated with the extent of sites-specific inflammation of the periodontitium, information about PGE_2 levels in gingival fluid may not be predictive of future periodontal conditions (Alexander et al, 1996; Leibur et al, 1999). Information about tumor necrosis factor alpha (TNF-α) may also be of diagnostic importance but there are no data available on the long-term usefulness of information on TNFα in PRM. Plasminogen activation is a key element in controlling proteolytic events in the extracellular matrix. Information about tissue-type plasminogen activator (t-PA) and plasminogen activator inhibitor-2 (PAI-2) is commonly used is risk assessment for other systemic conditions, i.e. severe heart disease, and may also be useful for periodontal risk prediction (Yin et al, 2001). Matrix metalloproteinase-3 (MMP-3) and tissue inhibitor of metalloproteinases-1 (TIMP-1) in gingival crevicular fluid (GCF) are other markers of inflammation that in the future may serve as prognostic factors for the progression of periodontitis (Alpagot et al, 2001).

One of the major problems with such markers of inflammation is that they require laboratory assay methods and provide no immediate clinic information. Collection of gingival crevicular fluid is often included in such assay methods. This makes it difficult to assess disease risk at the patient level.

Use of Anti-inflammatory Agents

There is currently limited information on the use of anti-inflammatory agents, i.e. non-steroidal drugs and their efficacy in the management of periodontitis in humans.

In summary:
- immunity factors are important in the host defense against periodontitis
- studies of immune functions relative to treatment outcomes have not progressed to the point where such information provides value for PRM
- a vaccine against periodontitis is not available
- site-specific markers of inflammation have been of scientific interest, but limited information is available justifying the use of such assays for the prediction of periodontitis and use in long-term PRM
- there is limited information about the efficacy of anti-inflammatory drugs against periodontal inflammation and such drugs may be of limited value in PRM.

5) THE ROLE OF EXTRINSIC INFLUENCE OF SOCIAL AND BEHAVIORAL FACTORS IN PRM

Several extrinsic factors have been identified as potential risk factors that should be considered in PRM. Some factors are poorly investigated such as the role of nutrition as a periodontal risk factor whereas other factors have been exposed to extensive interest, i.e.: 1) smoking; 2) socio-economic factors; 3) behavioral; 4) stress; 5) psychological factors; 6) access to dental care; and 7) compliance with SPT protocols.

Smoking as a Factor

Many studies have identified associations between smoking habits, poor oral hygiene and periodontitis (i.e. Pindborg, 1949; Ismail et al, 1983; Bergström, 1989; Preber and Bergström, 1985, 1990; Haber et al, 1993). The NHANES III data suggest that the risk for periodontitis in smokers versus nonsmokers is 4:1 (Tomar et al, 2000). Smoking has an impact on hemorrhagic responsiveness in that bleeding on probing is reduced thereby masking the clinical impression of inflammation (Bergström and Boström, 2001). It has also been shown that smoking will negatively affect the treatment outcome after scaling and root planing (Preber and Bergström, 1990), modified Widman flap surgery (Preber and Bergström, 1990), and regenerative periodontal therapy (Tonetti et al, 1995).

Data at reevaluation and during a 6-year period of supportive periodontal therapy (SPT) have shown that smokers display less favorable healing responses (Kerdvongbundit and Wikesjö, 2002). Thus, the risk of clinical attachment loss may be at least twice as high among smokers in spite of participation in SPT (Calsina et al, 2001). It also appears that smokers have a 2.7 and former smokers a 2.3 times higher risk for periodontitis as compared to nonsmokers and with a dose (smoking) related effect (Amarasena et al, 2002). However, a large study of a Sri Lanka population has also demonstrated that tobacco smoking is not part of an explanatory model for periodontitis. Poor oral hygiene alone explains 46% of periodontitis while smoking only accounts for 7% and is not statistically significant (Ogawa et al, 2002). Thus, it may take more than smoking alone to amplify the risk for periodontitis.

The impact of smoking cessation on the outcome of periodontal therapy has only been reported in a few studies and the data does not explicitly report that smoking cessation has an immediate significant impact on treatment efficacy, or periodontitis progression. A dose-response relationship between cigarettes smoked per day

Table 5 Selected studies providing odds ratios between smoking and periodontitis

Study Identification	Odds ratio	95% CI	Remarks
Ogawa et al, 2002	3.7	1.4 – 9.9	Older subjects (n = 599) at baseline and 394 at two years and clinical attachment loss during two years. No treatment performed. Longitudinal case control study
Müller et al, 2002	1.9	1.2 – 2.9	Young adults (n = 65) development of bleeding on probing during 24 months of military service. Short longitudinal case control study
Van Winkelhoff et al, 2001	13.8		Presence of *F.nucleatum* and *M.micros* in pockets of smokers/ non-smokers (n = 468). Cross-sectional case control study
Tomar and Asma, 2000	3.9 3.2 1.2	3.2 – 4.9 2.2 – 4.7 0.8 – 1.6	NHANES III (n = 12329) odds ratio that smokers had periodontitis. Former smokers (quit within 2 years) having periodontitis. Former smokers (quit > 10 years) having periodontitis. Cross-sectional survey
Norderyd et al, 1999	20.3	5.1 – 80.8	20 years longitudinal study (n = 474). Smoking and severe periodontitis. Longitudinal case control study
Machteii et al, 1998	5.4	1.5 – 19.1	Longitudinal study (n = 79) of subjects over 12 months with untreated periodontitis. Serum cotinine sign. elevated among subjects loosing clinical attachment. Odds that current smokers have clinical attachment
Moss et al, 1996	5.0	1.9 – 13.2	Cross-sectional study of 148 subjects with or without depression. Odds that current smoking is risk factor

and the reduced risk for periodontitis may require > 11 years (Bergström and Boström, 1998). Thus, short-term effects of smoking cessation may be difficult to interpret. A summary of studies providing odds ratios of associations between smoking and periodontitis is presented in Table 5.

Socio-economic, behavioral, stress, and access to dental care as factors in PRM

Studies of minority groups in the USA have shown that occupational status and ethnicity among unskilled subjects is associated with a high risk for periodontitis (Craig et al, 2001). A socio-ecological explanation of periodontitis has been identified suggesting short duration of education and poor oral hygiene being associated with more severe periodontitis (Hansen et al, 1995). Financial strain has been identified as a significant factor associated with alveolar bone loss (Genco et al, 1991). Such data are supported by findings from a 20-year longitudinal study in Sweden demonstrating that the odds of poor socio-economic status and having periodontitis was 8.5:1 (95% CI: 2.0-36.4) (Norderyd et al, 1999). Several difficulties exist in assessing periodontal conditions in low-income populations because many of these subjects are preoccupied with other needs and perceive dental care and oral health as low priorities and may not want to participate in any dental studies (Hanson and Persson, 2003). Thus, in order to become effective it is imperative that PRM takes into account specific approaches in management of low-income subjects to eliminate oral health disparity. Effective PRM may require public financial support (dental insurance), education of both the public and oral healthcare providers including dental and dental hygiene students. Improved access to care would also be necessary while PRM must also be effectively provided at low cost.

Psychological Factors in PRM

An association of risk for periodontitis has been reported for severe depression and presence of *T.forsythensis* in plaque samples (Moss et al, 1996). Such findings are consistent with reported refractory periodontitis in persons under stress and suffering from depression (Axtelius et al, 1998). Other studies have confirmed that psychosocial factors and oral health risk behaviors cluster together as important determinants of periodontitis (Croucher et al, 1997; Hugoson et al, 2002). Studies of

Table 6 Odds ratios and periodontitis based on socio-economic factors

Study Identification	Odds ratio	95% CI	Remarks
Borrell et al, 2002a,b	1.3	0.8 – 2.2	NHANES I odds of being black versus Caucasian and having periodontitis 1971 – 1974.
	2.1	1.7 – 2.6	NHANES III odds of being black versus Caucasian and having periodontitis 1988 – 1994. Notice increased risk over time
Elter et al, 2002	2.2	1.1 – 4.6	Odds of having substandard periodontal treatment outcome in depressed subjects (n = 1299)
Tezal et al, 2001	1.4	1.02 – 1.80	Odds of having clinical attachment loss if drinking > 10 alcoholic beverages per week (n = 1371). No association to alveolar bone loss
Norderyd et al, 1999	8.5	2.0 – 36.4	20-year longitudinal study (n = 474). Socioeconomic status associated with severe alveolar bone loss.
	3.2	1.0 – 10.0	Female gender associated with severe bone loss

psychosocial measures of stress and periodontitis have shown that financial strain and distress that may manifest itself as depression are significant risk indicators for more severe periodontal disease (Moss et al, 1996). In an age-adjusted model analysis gender (male), smoking, diabetes mellitus, *T.forsythensis*, and *P. gingivalis* were also significant risk indicators (Mos et al, 1998). The relationship between economic factors, stress and periodontitis may also explain why single living older subjects also appear to be at higher risk for periodontitis than older couples (Gelskey et al, 1998). A summary of odds ratios and risk for periodontitis based on socio-economic end ethnic factors is presented in Table 6.

In summary:
- subjects who smoke and have poor oral hygiene have an elevated risk for periodontitis
- former smokers may not reduce short-term risks for periodontitis and it may take years before the effect of smoking cessation results in significantly reduced risks for periodontitis
- low socio-economic status can be associated with increased periodontitis risk
- the evidence base that management of depression would reduce the risk for periodontitis is limited
- several confounding factors exist.

6) THE ROLE OF SYSTEMIC DISEASES AND PERIODONTITIS IN PRM

During recent years several reports have been published describing relationships between having periodontitis and also systemic disease. Such efforts have been focused on diseases such as: pre-term birth and low birth-weight and periodontitis, diabetes mellitus and periodontitis, cardiovascular diseases/stroke and periodontitis, osteoporosis and periodontitis, osteo-arthritis and periodontitis, depression and periodontitis. A review of the associations between these diseases and periodontitis is presented in another report (Renvert, 2003).

The focus of this research effort has predominantly been targeted towards the risk of having periodontitis affecting the onset and severity of other diseases. However, the reverse of this hypothesis has not been considered at length. Furthermore confounding factors have been identified and such factors may be of great significance in the development of both systemic and oral disease simultaneously without a direct cause and effect relationship. It seems reasonable that in any assessment of periodontal risk several systemic diseases should be considered as modifying risk factors. Thus, it would be necessary to consider the effects of medications such as diuretics and blood pressure controlling agents, immunosuppressive drugs, anti-inflammatory drugs, hormonal replacement drugs, bone metabolism drugs, and nutrition supplements. Whether or not routine periodontal therapeutic procedures are effective in inreducing overall disease risk subjects with such conditions, is currently difficult to evaluate as the evidence base does not exist.

The development of periodontal medicine is relatively new. The appreciation that periodontitis may have an impact on systemic health or the reverse has not been considered in preceding studies assessing periodontal conditions or treatments including aspects of PRM. Oral

healthcare providers must therefore consider systemic conditions and drug interactions in PRM and seek consultations with physicians.

In summary:
- diseases that may have shared etiology, genetic, and socio-behavioral factor with periodontitis include:
  - diabetes mellitus,
  - cardiovascular diseases including stroke
  - osteoarthritis
  - depression
  - low birth weight.

7) THE PREDICTIVE VALUE OF ROUTINE CLINICAL PARAMETERS IN PRM

Management

The assessment of the predictive value of certain cut-off levels for routine clinical periodontal parameters including information on bleeding on probing, probing depth, clinical attachment levels, and evidence of alveolar bone loss as assessed from radiographs is limited by the fact that a vast majority of studies have only considered site-specific data disregarding subject specific influences on the outcome of care or progression of disease.

Probing Depth

On a site basis, there are many studies demonstrating that both surgical and non-surgical procedures are predictive in reducing probing depths and that SPT can effectively prevent recurrence of deeper periodontal pockets (i.e. Knowles et al, 1979; Badersten et al, 1985a, b; Kaldahl et al, 1996; Claffey et al, 1990). However, these studies are limited in that they do not necessarily present data on teeth extracted and the impact on study outcomes from subject dropout or case selection mechanisms. A recent systematic and subject and evidence-based review of the literature on the value of remaining probing depths ≥ 6 mm after ICRT yielded only one study (Renvert and Persson, 2003). However, the study by Claffey and Egelberg (1995) demonstrated that remaining probing depths ≥ 6.0 mm after completion of ICRT has a negative predictive value. Thus, with an increasing number of teeth with deep probing depths after ICRT the greater the risk for progressive periodontitis (subject-based data). In a retrospective study of subject-based data over eight years among compliant subjects only the baseline number of remaining teeth and the number of SPT visits was related to tooth loss (König et al, 2002).

Recent statistical analysis of the role of baseline probing depth in assessment of outcomes has demonstrated that there is a strong probability of obtaining statistically significant correlation/regression coefficients as an artificial effect of mathematical coupling from the true underlying biological relationship. Therefore, it may be necessary to use new and revised appropriate analytical strategies and to re-evaluate previous 'evidence' within the periodontal literature on the role of probing depth (Tu et al, 2002). This would also apply to other clinical factors commonly studied in periodontal research. Thus, the relevance of specific clinical periodontal findings may have been overstated.

Bleeding on Probing

Bleeding on probing reflects one of the cardinal signs of inflammation and information on gingival bleeding is commonly used in gingival indices (not referenced here but part of, i.e. the Löe-Silness index, the Ainamo-Bay index, the PMA index, and the CPITN/PSR index). Assessment of bleeding on probing is a routine clinical procedure and also often used as an outcome measure in combination with drug interventions. Absence of bleeding following probing has been associated with stable periodontal conditions (Lang et al, 1990), whereas repeat bleeding occurrences at different times suggest unstable periodontal conditions and risk for further attachment loss almost suggesting a 'dose-response curve'. If, after non-surgical ICRT a large number of sites continue to bleed, one may expect an increased number of sites positive for *P. intermedia/nigrescens* (Mombelli et al, 2000).

However, it may be difficult to separate out the independent role of bleeding on probing in assessing the progression of periodontitis because bleeding on probing and probing depth may not be independent factors. Furthermore, drug interactions may further complicate assessments of periodontal status based on information about bleeding on probing. For example, aspirin is increasingly used in the prevention of cerebro-vascular and cardiovascular diseases and is a non-disease factor that may modify bleeding indices given its anti-thrombolytic activity (Schrodi et al, 2002).

Radiographic Evidence of Alveolar Bone Loss

Dental radiographs provide a hard copy of information obtained at a specific time point. Different sets of radiographs over time provide documentation of changes in bone density and signs of alveolar bone loss. However, radiographic data can only provide evidence of result of a past history of periodontitis. There are studies to suggest that radiographic evidence of bone loss is correlated with clinical measures (Hämmelie et al, 1999; Zybutz et al, 2000). The link between changes in clinical attachment and alveolar bone height is complex, perhaps because changes in the two tissue types are sepa-

rated by a considerable time delay (Pilgram et al, 1999). The role of age in alveolar bone loss is unclear. Studies of subjects between the ages of 20 and 64 have revealed that age-related alterations in the periodontium may not inevitably be manifested as loss of probing attachment or loss of alveolar bone (Papapanou et al, 1991; Papapanou and Lindhe, 1992).

Most commonly, the extent of alveolar bone loss (assessed as the distance between the cement-enamel junction (CEJ) and bone level (BL) is measured at the mesial and distal surfaces of teeth either directly from the radiographic film with a gauge device or from radiographic images that are first digitized and then analyzed aided by a computer software program (i.e. Brägger et al,1988; Akesson et al, 1992). The proportional relationship between root length and the distance between CEJ to BL has also been used for analysis of periodontal disease severity (Michalowicz et al, 1991). Studies have demonstrated that a distance between CEJ and BL exceeding 4.0 mm would constitute a reasonable threshold value above which any bone height value could be considered as abnormal (Papapnou et al, 1991; Persson et al, 1998). Among a large number of clinical variables it was recently demonstrated that periodontists predominantly use radiographic information in assessing risk for future periodontitis (Persson et al, 2003a).

Supportive Periodontal Treatment

In principle the rationale for three-month recall intervals for maintenance care is based on clinical studies with study protocols requiring clinical measurements with 3 – 4 month intervals (Knowles et al, 1979; Badersten et al, 1985a,b; Claffey et al, 1990; Claffey and Egelberg, 1995; Persson et al, 1998; Becker et al, 1984; Rosling et al, 2001; Serino et al, 2001). Another rationale for short intervals between clinic visits is the understanding that frequent maintenance care is necessary to eliminate/reduce sub-gingival proportions of pathogens associated with periodontitis. Recolonization of pathogens previously treated periodontal pockets occurs quickly if oral hygiene is not properly enforced (Magnusson et al, 1984; Sbordone et al, 1990). Therefore, three to four month maintenance care intervals have been suggested (Wilson, 1996). Yet another reason for three to four month intervals is that it provides the care provider opportunities to reinforce oral hygiene (Axelsson and Lindhe, 1981).

It is generally thought that regular maintenance care is essential for the long-term successful results of periodontal therapies. However, studies have also demonstrated that the compliance with attendance varies between 26% and 77% (Ojima et al, 2001; König et al, 2002; Demetriou et al, 1995; Mendoza et al, 1991). Contrary to current paradigm there are studies to support that it may be possible to maintain successful results of periodontal therapy in patients with less personal and professional efforts than traditionally recommended (Johansson et al, 1984). Thus, studies have demonstrated that irregular dental attendees do not have a higher prevalence or severity of periodontitis than patients who seek regular care (Mulally et al, 1994). Economic problems and fear of dental treatment procedures, have been identified as factors keeping patients from complying with scheduled recall intervals (Wilson, 1996).

Tooth Loss as an Indicator of Risk to be Considered in PRM

The ultimate outcome goal of preventive dentistry and care for patients with oral diseases is to preserve a functional complete dentition with no clinical evidence of disease. Various clinical parameters have been used to assess the outcome of care and where loss of individual teeth or the full dentition can be viewed as the terminal outcome of disease. In order to assess the risk of tooth loss as a consequence of periodontitis it is important to realize that teeth can be lost due to many factors including trauma, caries, failing endodontic treatment, cancer, as well as to failing periodontal treatment. Practical clinical reconstructive considerations and treatment strategies may require extraction of teeth otherwise without pathology but irrelevant to keep. There is currently little to no evidence from prospective studies that routine clinical periodontal measures are useful in predicting future tooth loss. In fact, many traditional prognostic factors are ineffective or irrelevant in predicting future bone loss. In a five year prospective study of 1101 older subjects preliminary results suggest that subjects who have fewer (< 17 teeth) are at greater risk of loosing additional teeth than those who have 28 or more teeth (Persson et al, 2003). However, periodontitis could only be identified as the rationale for tooth extraction in less than 20% of all tooth losses experienced in this study population.

Several retrospective studies have evaluated the effectiveness of ICRT followed by SPT (i.e. Axelsson et al, McLeod et al, 1998; Rosling et al, 2001; Serino et al, 2001). The use of systemic antibiotics as an adjunct to non-surgical SPT may effectively reduce the needs for tooth extractions (Loesche et al, 2002). Whether ICRT includes surgical treatment or not in patients referred to as downhill cases does not seem to have an impact on future tooth loss (McLeod et al, 1998). However, periodontal therapy itself may often include tooth extraction as part of treatment (Kaldahl et al, 1996). Studies of dental insurance claims suggest that periodontal therapy over three years can reduce tooth loss risk by 58% and that non-surgical periodontal therapy effectively prevents tooth loss (Hujoel et al, 1999, 2000). In one study, subjects with moderate periodontitis who after ICRT only partially complied with SPT experienced on average a loss of 0.9 teeth per subject over periods up to 17 years

Table 7 Data on tooth loss and cause of extractions from selected studies

Study Identification	Type of study	ICRT	Tooth loss	Cause for extraction
König et al, 2002	10-year retrospective University based study of compliant subjects (n = 142)	Surg. and non-surg. periodontal TX and SPT as needed	During ICRT: 167 teeth extracted during SPT: 99 teeth extracted. 10 independent variables explained 9% of cause for tooth loss	ICRT: Periodontitis 82% Reconstructive 12% SPT: Periodontitis 48% Endodontic: 30% Reconstructive: 14%
Checci et al, 2002	Retrospective study over 4 years or more of 92 subjects in private practice	Surg. and non-surg. periodontal TX assessed prognosis after ICRT: Good 64.6% Hopeless 8.9% Assessed prognosis after SPT: Good 68.2% Hopeless 7.8%.	During ICRT 126 (5.5%) teeth extracted. During SPT: 50 (2,2%) teeth extracted	88% of teeth lost during SPT due to periodontitis. Group with good baseline prognosis lost 1 tooth/1405. Group with questionable prognosis lost 21/557 teeth (3.8%). Group with poor prognosis lost 22/172 teeth (12.8%)
Rosling et al, 2001	12-year retrospective study of 225 subjects with normal and 109 subjects with high periodontitis risk in SPT programs in Dental Public Health Clinics	Surg. and non-surg. therapy as indicated SPT on individual needs	During SPT 64% of subjects in high risk group lost teeth (on average 1.9 teeth/subject). 26% in low risk group lost teeth (on average 0.3 teeth/subject)	Cause for tooth loss not reported
Kocher et al, 2000	10-year retrospective University based study of 572 patients with periodontitis	Surg. and non-surg. periodontal TX. 257 subjects dropped out of study (group A) 160 subjects non-compliant (group B) 155 completed TX (group C)	Total extractions Group A: 16% Group B: 14% Group C: 8% During SPT: Group A: 13% Group B: 13% Group C: 4%	Study limitation: Group A represented by 14 subjects. Group B represented by 26 subjects. Group C represented by 27 subjects. Cause for extractions not reported
Tonetti et al, 2000	Retrospective University based study of 273 subjects with periodontitis	Surg. and non-surg. periodontal TX	Extractions ICRT: 5.2% SPT: 4.4%	Cause for extractions: Periodontitis 57% Caries/endo/technical 29% Perio-combined 14%

(Moser et al, 2002). Thus, exclusive information about SPT compliance alone may not be informative in assessing risk for future tooth loss. Additional data from select studies are presented to further elucidate the ability to predict future tooth loss (Table 7).

The complexity of PRM to prevent tooth loss can also be demonstrated by the poor predictability of assigned risk scores (questionable or poor prognosis) on a tooth basis (McLeod et al, 1998). Thus, in this study of periodontal treatment outcome of 114 subjects with at least five years of SPT the ability to predict tooth loss based on a questionable prognosis assignment was 14%, whereas for hopelessly assigned teeth the prognostic ability was 33%. These findings are consistent with other studies demonstrating that the ability to predict worsening periodontal conditions for teeth with initial assignment of questionable or poor prognosis is approximately 50% (McGuire and Nunn, 1999). Furthermore expert clinicians do not necessarily agree on periodontal risk assignments (Persson et al, 2003).

Table 8 Scoring characteristics for the multi-functional Periodontal Risk Assessment (PRA)

Score	Bleeding on Probing	N of sites PPD ≥ 4 mm	Tooth loss	Bone loss/age	Smoking	Genetic Systemic
2	0 – 9%	≤ 2	≤ 2	≤ 0.25	No smoking a score of 1	Negative score of 0
4	10 – 16%	3 – 4	3 – 4	0.26 – 0.49	Former smoking	
6	17 – 24%	5 – 6	5 – 6	0.50 – 0.79	1 – 9 cig./day	Positive Score of 10
8	25 – 36%	7 – 8	7 – 8	0.80 – 1.00	10 – 19 cig./day	
10	36%	> 8	> 8	> 1.0	≥ 20cig./day	

In summary:

- clinical measures of bleeding on probing and pocket depths may have limited value in assessing periodontal disease risk
- dental radiographs can be used to identify past history of disease
- dental radiographs cannot predict future periodontal disease
- SPT has for many years been considered as essential for successful ICRT
- the significance of non-compliance as a risk for recurrent disease may have been overstated or at least not thoroughly considered
- subjects who might be at most risk for periodontitis are also the non-compliant subjects
- routine measures of clinical conditions may not be predictive
- tooth loss may not be prevented by SPT, but the extent of complience may predict further tooth loss
- SPT should be individualized based on assessed risk of disease recurrence.

8) A MODEL FOR PERIODONTAL RISK ASSESSMENT

This report has pointed out a large number of individual factors that have been used for the purpose of predicting future risk for periodontal disease. A comprehensive approach to risk assessment, which could result in effective PRM has rarely been attempted. However, recently two models for such analysis have been published (Lang and Tonetti, 2003b; Persson et al, 2003b). In a functional risk diagram information about the proportion of sites with bleeding on probing, the number of teeth/sites with probing depth ≥ 5.0 mm, the number of teeth lost previously, the extent of alveolar bone loss, information about genetic and systemic factors (i.e. Il-1 gene polymorphism, diabetes mellitus, cardiovascular diseases, and smoking habits), and other environmental factors has been used (Lang and Tonetti, 2003). Thus, this functional periodontal risk assessment (PRA) model has demonstrated that subjects enrolled in a SPT program do not respond favorably to SPT if they carry the Il-1-1 gene positive haplotype. In the other model a large number of clinical factors including measures of bone loss, probing depth, bleeding on probing, previous oral hygiene habits, systemic disease, self-perception of disease risk has been used in the development of a computer software program for risk assessment (Persson et al, 2003a). Studies of the computer software program (Risk calculator) have only been performed to assess the agreement between expert clinical opinion and the software program and between clinicians with different periodontal training. In both cases further studies are needed to evaluate such models for risk assessment.

The PRA model utilizes information from several of the factors discussed in this document including: 1) number of sites with bleeding on probing; 2) number of pocket depths ≥ 5.0 mm; 3) number of teeth lost; 4) alveolar bone loss (genetic and systemic disease factors; and 5) smoking and environmental factors. The risk threshold values used for the PRA are presented in Table 8. An illustrative example of the PRA is shown in Fig 1. It is either possible to count the number of vectors with a certain score (Lang and Toneti, 2003) or to calculate the surface area encompassed by the scores for each parameter and then use change of surface area as an indication of improvement or deterioration (Persson et al, 2003).

A case example of the PRA is presented (Figs 2 and 3). Following ICRT this 38-year-old male was transferred to a SPT program scheduled in such a way that if the PRA diagram suggested a high risk the patient would be seen in SPT more frequently. Thus, the intervals varied. Over

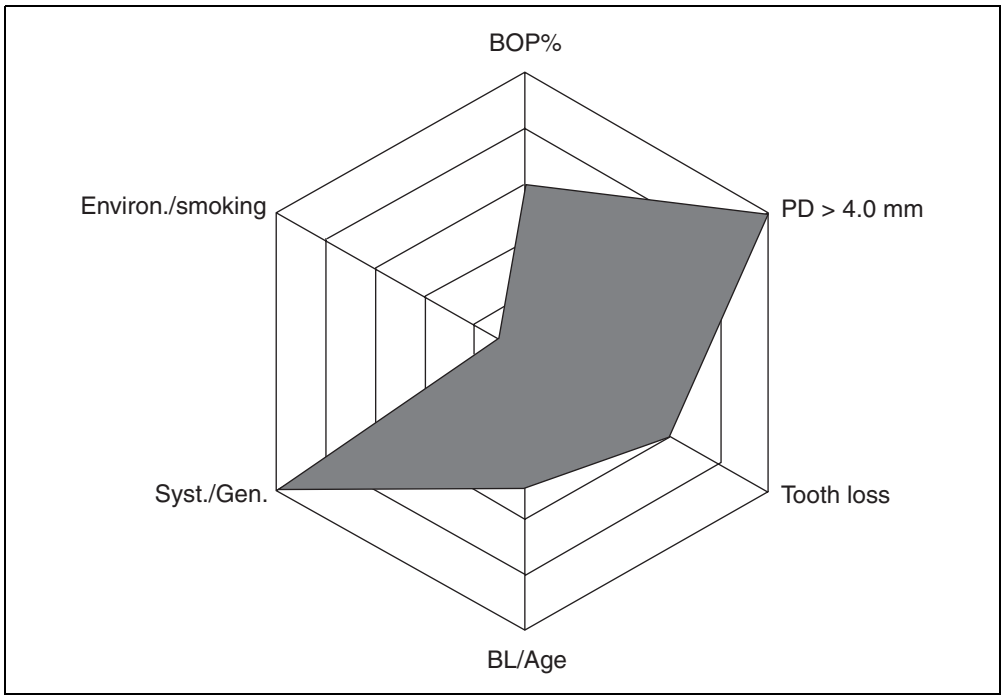

Fig 1 Functional Risk Diagram with three of the risk indicator scores at the '8' level or more suggesting high risk. Only the bleeding on probing indicator can be reduced to a lower level by treatment.

a three-year period the patient was treated in the SPT program 11 times. At baseline this subject smoked a pack of cigarettes every day and did not change his smoking habit. Hence he scored at '10' both at baseline and at visit 12. The patient was interleukin 1-gene polymorphism positive, a factor that could not be changed over time. Thus, he scored '10' at all times for the genetic/systemic factor. At the worst tooth site the extent of age adjusted bone loss was 0.4 suggesting a low risk of bone loss and a score of 4. This factor remained the same over the three years. He had lost 11 teeth in the past, which was another factor that could not be changed but he lost no more teeth during the follow-up period. The number of tooth/sites with a probing depth ≥ 5.0 mm was at baseline 11 thus yielding a score of '10'. At year three he only had 2 sites with a probing depth ≥ 5.0 mm. At the first visit 21% of sites bled on probing while at visit 12 only 4 sites bled. The surface area circumscribed by the six vectors was calculated using Microsoft excel software. At baseline the 'surface area risk score' was 113.5 and changed to 77.1 at visit 12. Thus, by comparing surface area as a method to assess change of risk it was possible to demonstrate that this patient had a reduced risk for periodontitis at visit 12 of SPT. However, three vectors, two of which cannot be changed remained as high risk indicators. The only factor that can be worked on in PRM would be the smoking status of the subject. Thus, the diagram provides visible guidance on what factors might be manageable in PRM.

OVERALL CONCLUSIONS ON PRM

- A large number of extrinsic factors have been associated with a risk for periodontitis.

Currently valuable conditions in PRM:

- the presence of a cluster of pathogens has been associated with periodontitis and may predict a risk for periodontitis activity and should therefore be managed
- smoking habit appears to be a major risk factor but smoking must be carefully evaluated as the impact of smoking secession and immediate reduced risk for periodontitis remains unclear
- a past history of tooth loss may be predictive of future tooth loss and useful information in PRM
- socio-economic and behavioral factors are of importance in risk assessment but most likely very difficult to affect in order to manage periodontal risk
- systemic or oral health management should be coordinated as there appear to be several shared risk factors.

Conditions that may contribute to PRM but would require additional documentation are:

- there are no definitive answers on the role of mechanical and/or adjunct use of antibiotics to reduce/eliminate pathogens in the long-term management of periodontal risk

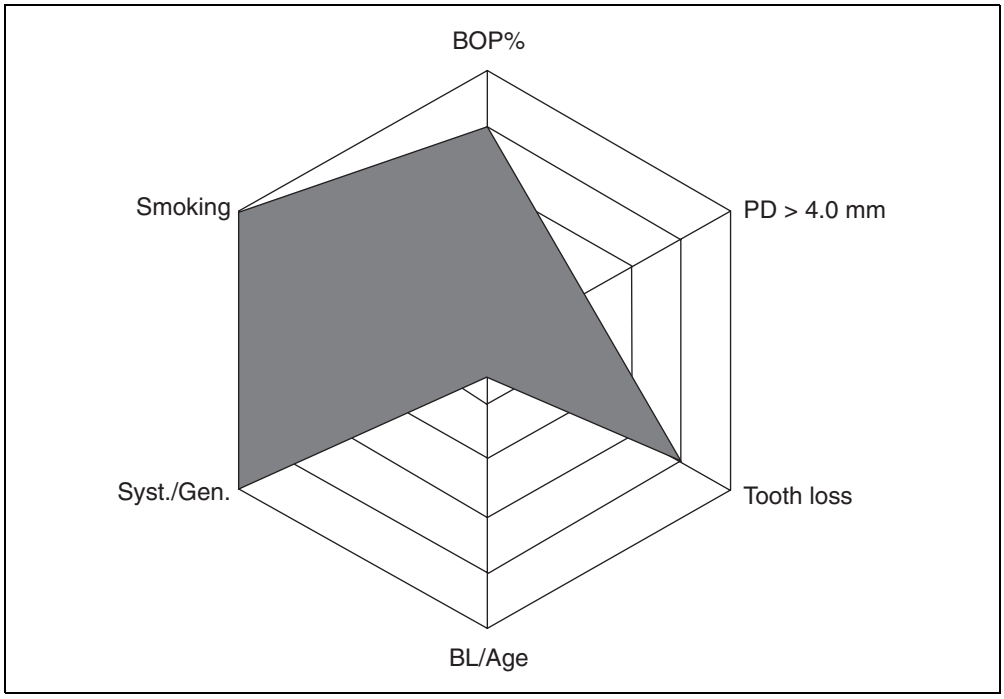

Fig 2 Example of PRA at first SPT visit.

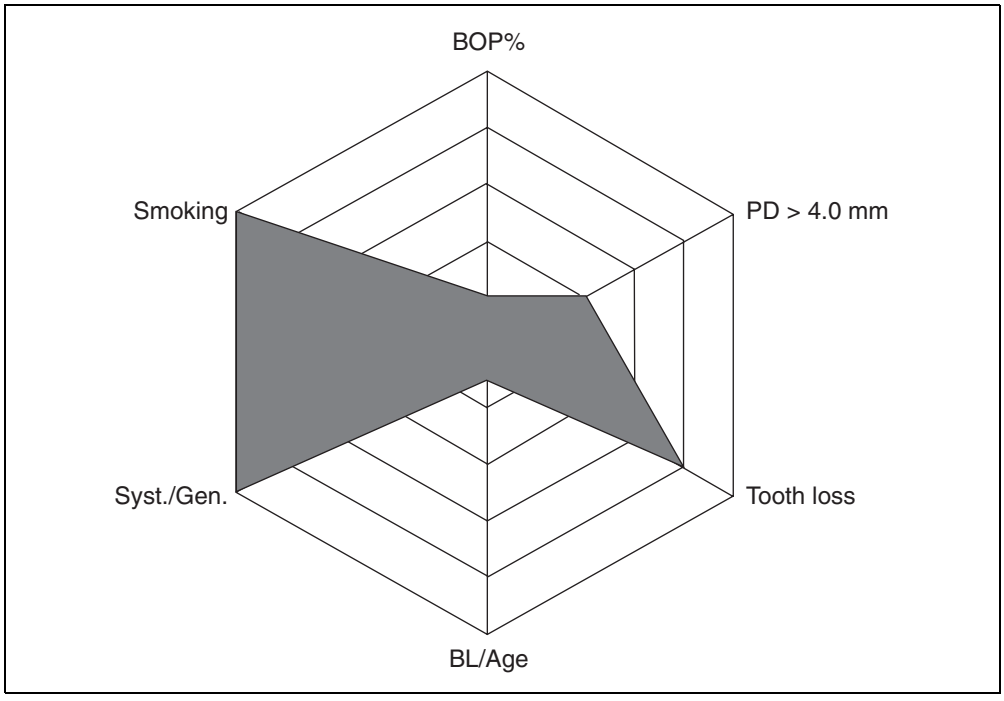

Fig 3 PRA diagram at the 12th SPT visit.

- genetic factors appear to be of importance for the regulation of host immune responses to infection and explanatory to current and future periodontitis risks but gene therapy is not available to manage genetic risk factors for periodontitis
- information on the presence or absence of serum or gingival fluid antibodies to periodontal pathogens, and cytokine levels is not exclusively predictive of periodontitis
- routine clinical measures of periodontal status provide information about current conditions but yield limited information for the long-term strategy for PRM.

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