Case Report/Series

Diagnosis of Stage III Periodontitis and Ambiguities of the "Gray Zones" in Between Stage III and Stage IV

Benyapha Sirinirund DDS[*], Riccardo Di Gianfilippo DDS[†], Shan-Huey Yu DDS, MS [‡], Hom-Lay Wang DDS, MSD, PhD [§], Kenneth S. Kornman DDS, PhD [‖]

[*] Resident of Graduate Periodontics. Department of Periodontics and Oral Medicine, School of Dentistry, University of Michigan, Ann Arbor, Michigan, USA.

[†] Resident of Graduate Periodontics. Department of Periodontics and Oral Medicine, School of Dentistry, University of Michigan, Ann Arbor, Michigan, USA.

[‡] Clinical Assistant Professor at Graduate Periodontics. Department of Periodontics and Oral Medicine, School of Dentistry, University of Michigan, Ann Arbor, Michigan, USA.

[§] Professor and Director of Graduate Periodontics. Department of Periodontics and Oral Medicine, School of Dentistry, University of Michigan, Ann Arbor, Michigan, USA.

[‖] Adjunct Clinical Professor at Graduate Periodontics. Department of Periodontics and Oral Medicine, School of Dentistry, University of Michigan, Ann Arbor, Michigan, USA.

Corresponding author:

Hom-Lay Wang, DDS, MSD, PhD

Department of Periodontics and Oral Medicine, University of Michigan School of Dentistry

1011 North University Avenue

Ann Arbor, Michigan 48109-1078, USA.

TEL: (734) 763-3325; FAX: (734) 936-0374

E-mail address: homlay@umich.edu

Word count: 1921

Figures: 2

References: 5

Short running title: Diagnosis of gray zone Stage III periodontitis

One sentence summary: Credible clinical judgment is needed to differentiate between Stage III and Stage IV periodontitis.

Disclaimers: The authors do not have any financial interests, neither directly nor indirectly, with the information included in the paper. No funding was available for this study. All the authors report no conflict of interest related to the study.

Authorship:

BS, RDG, SHY, HLW and KK: Case documentation, manuscript preparation and final
approval of the manuscript.

ABSTRACT

Introduction: How to best classify the Stage III and IV periodontitis cases that share
common features of the most severe clinical attachment loss and the most severe
radiographic bone loss?

Case Presentation: Two patients presented features of generalized periodontitis, with
severe probing depth and clinical attachment loss that would meet inclusion in both Stage III
and IV. The cases retained all teeth but were further complicated by teeth drifting and
secondary occlusal trauma. Appropriate disease classification required clinical judgement
and led to the final classification of Stage III, Grade C for both cases.

Conclusion: Patient-based clinical judgement, aiming for long-term preservation of natural
dentition, drives the final assignment of staging when the case falls in the "gray zone" that
focuses on major differences in Stage III and IV periodontitis.

Key words: Disease Progression, Periodontitis, Prognosis, Risk Factors, Tooth Loss, Periodontal Attachment Loss.

Exemplary Figures: Figure 1a, Figure 2a.

BACKGROUND

Medical classifications are utilized to transform clinical data into diagnostic categories that guide the diagnosis for a specific patient, assist treatment planning, and estimate short- and long-term prognosis. The classification of periodontal diseases evolved over the decades to reflect our knowledge and understanding of the disease pathogenesis. The 1999 World Workshop on the Classification of Periodontal Diseases and Conditions emphasized the distinction between Chronic and Aggressive Periodontitis, that dominated clinical practices and much of periodontal research for two decades [1]. The 2017 World Workshop joined experts from the American Academy of Periodontology (AAP) and the European Federation of Periodontology (EFP), and recognized Periodontitis as one disease entity with a broad range of clinical presentations, i.e. phenotypes. The staging and grading system was adopted to bring multiple dimensions to help classify different clinical phenotypes to distinguish approaches to guide management of cases that require more advanced knowledge [2]. The newly developed classification matrix for periodontitis evaluates the severity and extent of the past destruction, the complexity of treatment, and potential risk for further progression. The periodontal community is undergoing the process of adaptation to the new system and exploration of "gray zone" cases that may produce uncertain clinical

scenarios in need of thoughtful clinical judgement [3]. A call for sharing experience and rationale on how to interpret the "gray zone" is needed and narratives have been published to guide clinicians on their interpretation and dissemination of the new classification [4,5]. Therefore, the aim of this article is to present two "gray-zone" cases that fall within Stage III and IV, and illustrates the decision-making process and the clinical judgment that was used to differentiate Stage III and Stage IV cases.

CLINICAL PRESENTATION

Patients were received at the Department of Periodontics and Oral Medicine, University of Michigan School of Dentistry. Both patients have electronically signed an informed consent for periodontal examination and treatment, and gave oral consent for the use of clinical, radiographic and photographic data for research purposes.

Case 1:

Patient E.G. is a 46-year-old Caucasian female who presented to the Department of Periodontics of the University of Michigan for consultation. Medical history revealed uncontrolled Type 2 diabetes mellitus (T2DM; HbA1c: 9.4%) and morbid obesity [body mass index (BMI): 50.6 kg/m^2]. Medications at the time of first examinations were Glargine Insulin[*], Dulaglutide[†] and Empagliflozin[‡]. The patient was a former smoker who used to smoke 10 cigarettes/day for 5 years and quitted 20 years ago. Clinical photos (Figure 1A) show the patient's deep overbite along with tooth drifting/flaring in the upper anterior sextant. Additionally, the patient had no missing teeth.

---

[*]Basaglar, Eli Lilly and Company, IN, USA

[†] Trulicity, Eli Lilly and Company, IN, USA

[‡] Jardiance, Boehringer Ingelheim Pharmaceuticals, Inc., CT, USA

The severity component of staging a case is based on the greatest interdental clinical attachment loss (AL) and radiographic bone loss (RBL). The notable periodontal (Figure 1B) and radiographic (Figure 1C) findings include: probing depths (PD) and AL up to 11mm (#5), and RBL to mid-third of root length or beyond, both of which qualify this patient for being classified as either Stage III or IV based on severity. In this case with no history of any tooth loss, the current severity based on AL and RBL is not under-estimated due to prior removal of any severely affected teeth. In cases where teeth have been removed, the remaining teeth often do not adequately represent the maximum severity of past destruction of periodontal supporting tissues.

Since the severity factors for this case differentiate Stage III and IV from Stage I and II, the primary challenge then becomes how to differentiate Stage III from Stage IV cases.

Stage III and Stage IV cases often include probing depths that exceed 5 mm, vertical bone loss of 3 mm or greater, and class II or III furcation involvement. Stage IV cases, however, are substantially more challenging to treat and often require interdisciplinary approach to reconstruct masticatory function and lost support for vertical dimension. The Stage IV cases often have fewer than 20 remaining teeth positioned as 10 opposing pairs and may have substantial tooth mobility of degree 2 and greater.

This case does have some drifting and flaring of maxillary anterior teeth but does not exhibit substantial loss of vertical dimension, substantial mobility, or masticatory dysfunction.

Although severe periodontitis is evident in this case, there is no clear indication of teeth having a hopeless status that would suggest periodontitis-driven tooth removal during initial phase of therapy. Considering that the patient did not lose any teeth due to periodontitis, and considering the current efficacy of periodontal regeneration for

infrabony defects, this case is more consistent with a Stage III than a Stage IV case (Figure 1D). Approximately 46% of this patient's teeth have AL of 6-11mm and >30% of teeth have severe RBL, indicating that the extent of severity and complexity of this case should be considered generalized Stage III.

Case management

The Grade for this case was derived primarily from the maximum RBL of approximately 60% of root length/age 46 = 1.3 ratio, indicating a relatively rapid past progression of bone and connective tissue destruction. The severe inflammatory tissue reaction despite the relatively low levels of plaque and calculus buildup, together with the uncontrolled T2DM (HbA1c: 9.4%) and severe obesity, which further supports a Grade C (Figure 1E), that identifies the patient as less likely to respond predictably to standard principles of periodontitis therapy and maintenance. All of the observations noted above lead to a final periodontitis classification for this case of Generalized Stage III Grade C Periodontitis.

Case 2:

J.V., a 34-year-old Caucasian female, presented at the University of Michigan for Periodontal consultation. Medical history was negative for any significant diseases or conditions except for obesity (BMI: 39.2 kg/m^2). The patient is a non-smoker. Currently, she takes no medication but claimed that she occasionally took the following supplements or medications: probiotics to better her immune system, Sertraline HCL[§] for her anxiety, Lansoprazole[**] for gastroesophageal reflux disease (GERD), melatonin to help her sleep,

---

[§] Zoloft, Pfizer Inc., NY, USA

[**] Prevacid, Takeda Pharmaceuticals U.S.A., Inc., MA, USA

Oxybutynin[††] for frequent urination. Clinical pictures (Figure 2A) showed no tooth loss and significant recession of the lower left central incisor (#24). Periodontal evaluations (Figure 2B) revealed PD and AL from 5 to 11mm, and radiographic bone loss (Figure 2C) extended to the mid-third of root and beyond, with vertical bony defects extending up to the apical third of the root (#24), generalized mobility with localized secondary occlusal trauma (#24, #25).

The clinical severity component of this case would qualify for Stage III or Stage IV periodontitis based on AL level and RBL extending to mid-third of the root and beyond (Figure 2D). Stage IV generally is differentiated from Stage III based on a sufficient number of missing teeth such that there is a loss of support for vertical dimension and substantial tooth mobility, drifting or flaring. Other factors that include probing depths that exceed 5 mm, vertical bone loss of 3 mm or greater, and class II or III furcation involvement do not differentiate Stage III or Stage IV.

Case management

Approximately 78% of the teeth exhibited AL ≥5mm, which contributes to a diagnosis of generalized periodontitis. Regarding the risk of progression, the high ratio of bone loss/age of 1.94 put this patient in Grade C category. After careful evaluation, the final periodontal diagnosis was determined to be Generalized Stage III Grade C Periodontitis. Despite absence of either of the grade modifiers diabetes and smoking, it was interesting to notice the significant inflammation characterizing the patient's periodontium (Figure 2E).

DISCUSSION

[††] Ditropan, Janssen Pharmaceuticals, Inc., NJ, USA

The primary goal of periodontal treatment is preservation of natural dentition in health, comfort, function, and esthetics [5], and is best achieved through an accurate diagnosis, treatment planning, regular maintenance, and long-term follow-up. The Staging and Grading system offers a guide for clinicians to highlight the important differentiating features of severe periodontitis cases that may have a major impact on treatment, monitoring, and efforts to identify systemic factors that may influence the patient's response to therapy. Solely considering the severity of disease presentation, both patients mentioned in this manuscript could be classified as either Stage III or IV. Despite the local factors that could affect complexity of the cases (teeth drifting for Case 1 and secondary occlusal trauma for Case 2) neither patient is likely to lose the whole dentition if properly treated with periodontal etiologic and corrective therapy. An additional factor that complicates the Staging diagnosis is the patient's perspective towards an extensive multidisciplinary plan. Despite that Case 1 experienced significant facial drifting of the whole anterior maxillary complex, the patient was not interested to start any orthodontic therapy to improve the occlusal scheme and re-establish a physiological overbite/protrusion. As the patient was considered not at risk of dentition loss without multidisciplinary care, the diagnosis was finalized as Stage III Periodontitis. However, if the patient had been interested to undergo orthodontic treatment, further intervention would have been needed and the patient diagnosis would then change to Stage IV due to the increased complexity of the overall multidisciplinary rehabilitation. Assigning Grade C for both patients entails additional evaluations in collaboration with the patient's physician to more accurately identify other risk factors that may influence other chronic inflammatory diseases that may be more predictive of progression of periodontitis. Uncontrolled diabetes mellitus of Case 1 significantly contributed to the imbalance between host immune response and the local resident microflora. Given current information on these patients, we will assume that the hyper-reactive tissue response featured by high inflammatory appearance despite low quantity of bacterial

debris was the main driver of progressive attachment loss. Case 2 did not present grade modifiers such as smoking and diabetes, and a more in-depth evaluation of genetic susceptibility, underlying systemic inflammation, and levels of C-reactive protein were suggested to better understand the origin of her increased susceptibility to rapid periodontal breakdown.

While in some cases it seems obvious from a clinical and patient perspective that a tooth needs extraction, in scenarios of generalized questionable periodontal prognosis clinicians and patients face the dilemma whether keeping or replacing a tooth will dramatically affect the overall periodontal-occlusal conditions. In these cases, defining a definitive prognosis as well as the best treatment plan appear a subtle task. It is important to keep in mind how the definition of periodontally hopeless tooth changed multiple times over the decades to reflect the advances in periodontal therapy, and how treatment for preservation of natural dentition still remains the primary goal of Periodontology [5]. In this line of thought, periodontal treatment of Generalized Stage III/IV Grade C Periodontitis requires significant clinical judgment to best determine the projected tooth prognosis, and the full-mouth implications that tooth preservation or extraction would provide to the patient seeking care at the periodontal office.

In conclusion, two cases were presented to guide the clinician to better diagnose periodontitis when the clinical appearance would clearly distinguish both cases as being Stage III or IV, but not Stage I or II. It was less clear, however, how one should clarify the distinctions in each of the two cases to guide a Stage III periodontitis classification. The strong distinction between Stage III and Stage IV involves clinical judgment on the implications of prior tooth loss and the near-term risk of losing additional teeth, while the rate of past progression together with grade modifiers guide a best estimate as to how the patient may respond to periodontal therapy based on standard principles of treatment and maintenance care.

Summary

Why are these cases new information?	• The present cases guide an accurate differentiation between Stage III and IV periodontitis, which greatly influences the treatment plan and is crucial for long-term success of periodontal therapy.
What are the keys for successful management of these cases?	• Accurate staging of a patient based on the following criteria: - the risk to lose more than 4 teeth, up to the whole dentition, - the need of complex multidisciplinary treatment plans for functional rehabilitation
What are the primary limitations to success in such cases?	• The distinction between Stage III and IV Periodontitis and an accurate assessment of Grade relies on the subjective evaluation of tooth prognosis, that might be biased by operator personal experience, training, knowledge and a patient's overall health orientation.

REFERENCES

1.   Armitage GC. Development of a classification system for periodontal diseases and conditions. *Ann Periodontol* 1999;4:1-6.

2.   Papapanou PN, Sanz M, Buduneli N, et al. Periodontitis: Consensus report of workgroup 2 of the 2017 World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions. *J Periodontol* 2018;89 Suppl 1:S173-S182.

3.   Kornman KS, Papapanou PN. Clinical application of the new classification of periodontal diseases: Ground rules, clarifications and "gray zones". *J Periodontol* 2020;91:352-360.

4.   Sanz M, Papapanou PN, Tonetti MS, Greenwell H, Kornman K. Guest Editorial: Clarifications on the use of the new classification of periodontitis. *J Periodontol* 2020;91:1385.

5.   Pini Prato GP, Di Gianfilippo R, Wang HL. Success in periodontology: An evolutive concept. *J Clin Periodontol* 2019;46:840-845.

Legend:

Figure 1. Case 1 clinical presentation and classification decision making

Figure 1a. Facial intraoral view divided by sextants.

Figure 1b. Initial maxillary and mandibular periodontal chart. Abbreviations. PD: probing depth. FMJ-CEJ: distance from the free gingival margin to the cemento-enamel junction. MGJ: distance from the mucogingival junction to the free gingival margin.
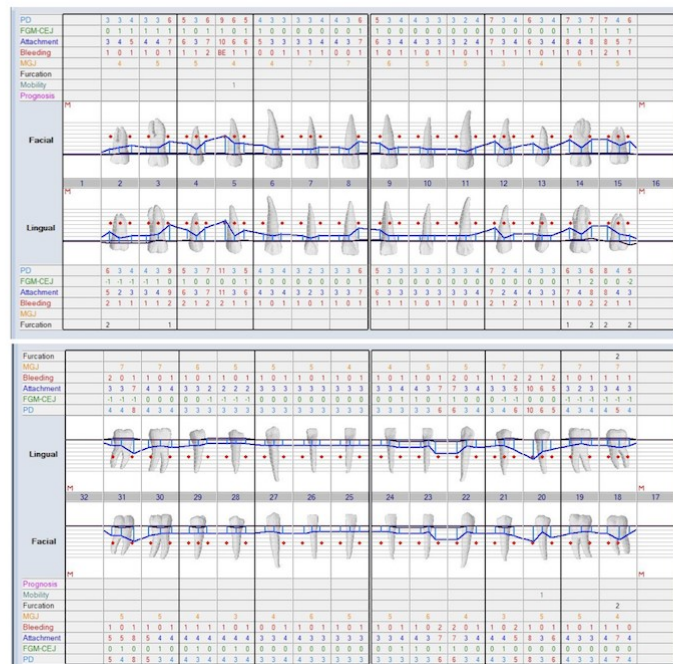

Figure 1c. Full set of intraoral periapical and bitewing radiographs.
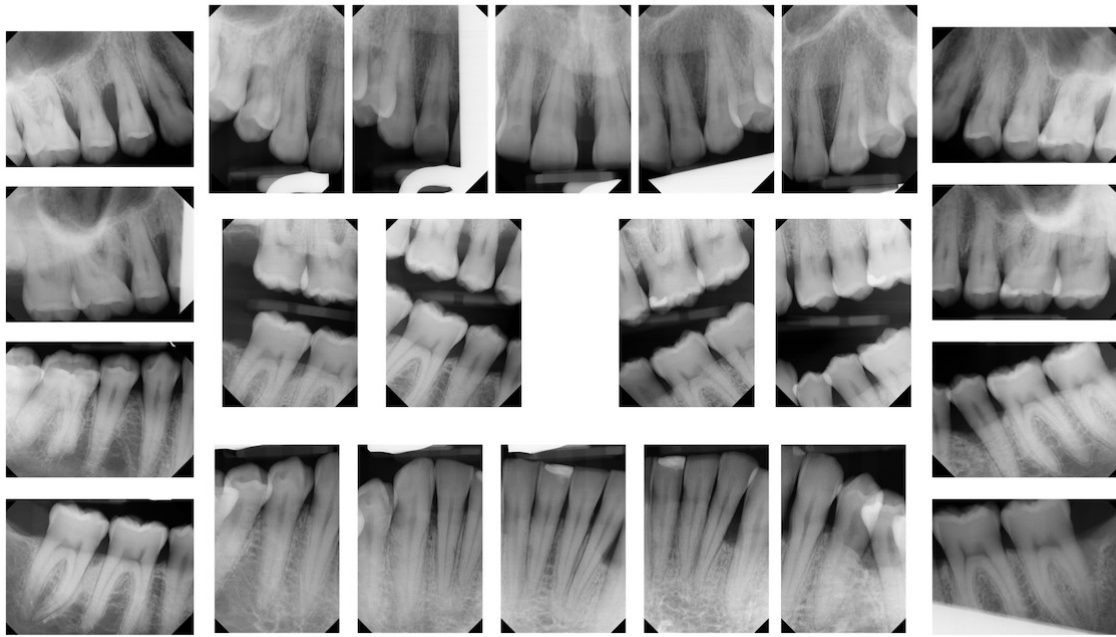
Figure 1d. Staging matrix as officially reported in the 2017 World Workshop[2].

Figure 1e. Grading matrix as officially reported in the 2017 World Workshop[2].

Periodontitis grade			Grade A: Slow rate of progression	Grade B: Moderate rate of progression	Grade C: Rapid rate of progression
Primary criteria	Direct evidence of progression	Longitudinal data (radiographic bone loss or CAL)	Evidence of no loss over 5 years	<2 mm over 5 years	≥2 mm over 5 years
	Indirect evidence of progression	% bone loss/age	<0.25	0.25 to 1.0	>1.0
		Case phenotype	Heavy biofilm deposits with low levels of destruction	Destruction commensurate with biofilm deposits	Destruction exceeds expectation given biofilm deposits; specific clinical patterns suggestive of periods of rapid progression and/or early onset disease (e.g., molar/incisor pattern; lack of expected response to standard bacterial control therapies)
Grade modifiers	Risk factors	Smoking	Non-smoker	Smoker <10 cigarettes/day	Smoker ≥10 cigarettes/day
		Diabetes	Normoglycemic/ no diagnosis of diabetes	HbA1c <7.0% in patients with diabetes	HbA1c ≥7.0% in patients with diabetes

Figure 2. Case 2 clinical presentation and classification decision making

Figure 2a. Facial intraoral view divided by sextants.

Figure 2b. Initial maxillary and mandibular chart. Abbreviations. PD: probing depth. FMJ-CEJ: distance from the free gingival margin to the cemento-enamel junction. MGJ: distance from the mucogingival junction to the free gingival margin.

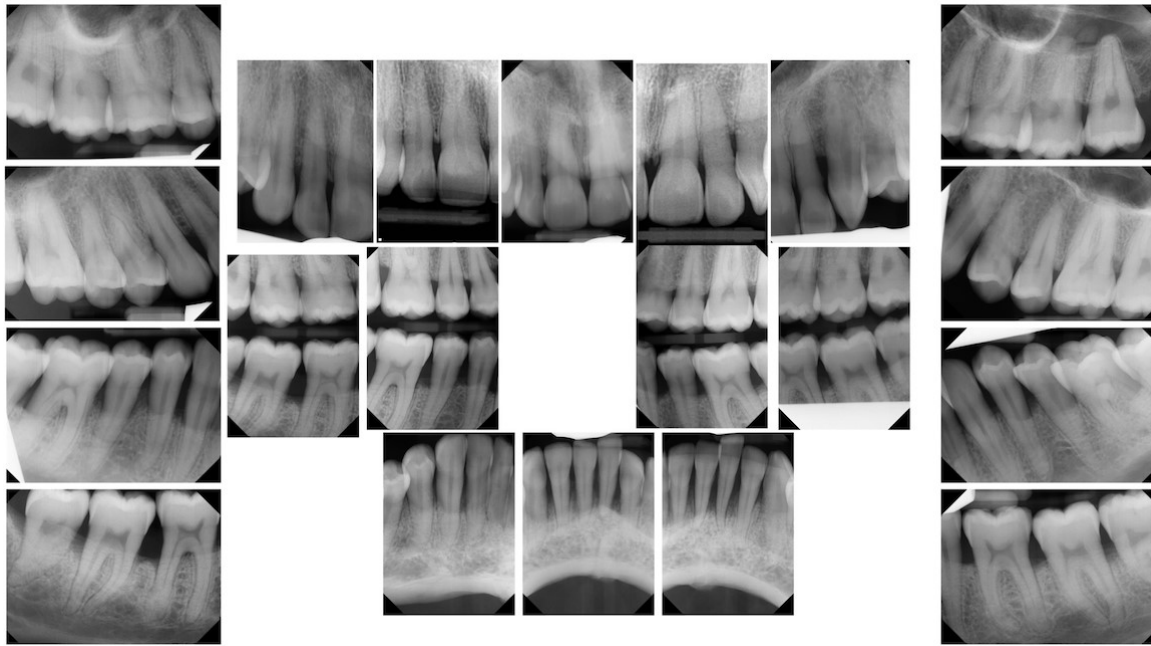Figure 2 c. Full set of intraoral periapical and bitewing radiographs.

Figure 2d. Staging matrix as officially reported in the 2017 World Workshop[2].

Periodontitis stage		Initial Periodontitis	Moderate Periodontitis	Severe with potential for tooth loss	Severe with potential for dentition loss
		Stage I	Stage II	Stage III	Stage IV
Severity	Interdental CAL at site of greatest loss	1 to 2 mm	3 to 4 mm	≥5 mm	≥5 mm
	Radiographic bone loss	Coronal third (<15%)	Coronal third (15% to 33%)	Extending to mid-third of root and beyond	Extending to mid-third of root and beyond
	Tooth loss	No tooth loss due to periodontitis		Tooth loss due to periodontitis of ≤4 teeth	Tooth loss due to periodontitis of ≥5 teeth
Complexity	Local	Maximum probing depth ≤4 mm Mostly horizontal bone loss	Maximum probing depth ≤5 mm Mostly horizontal bone loss	In addition to stage II complexity: Probing depth ≥6 mm Vertical bone loss ≥3 mm Furcation involvement Class II or III Moderate ridge defect	In addition to stage III complexity: Need for complex rehabilitation due to: Masticatory dysfunction Secondary occlusal trauma (tooth mobility degree ≥2) Severe ridge defect Bite collapse, drifting, flaring Less than 20 remaining teeth (10 opposing pairs)
Extent and distribution	Add to stage as descriptor	For each stage, describe extent as localized (<30% of teeth involved), generalized, or molar/incisor pattern			

Figure 2e. Grading matrix as officially reported in the 2017 World Workshop[2].

Periodontitis grade			Grade A: Slow rate of progression	Grade B: Moderate rate of progression	Grade C: Rapid rate of progression
Primary criteria	Direct evidence of progression	Longitudinal data (radiographic bone loss or CAL)	Evidence of no loss over 5 years	<2 mm over 5 years	≥2 mm over 5 years
	Indirect evidence of progression	% bone loss/age	<0.25	0.25 to 1.0	>1.0
		Case phenotype	Heavy biofilm deposits with low levels of destruction	Destruction commensurate with biofilm deposits	Destruction exceeds expectation given biofilm deposits; specific clinical patterns suggestive of periods of rapid progression and/or early onset disease (e.g., molar/incisor pattern; lack of expected response to standard bacterial control therapies)
Grade modifiers	Risk factors	Smoking	Non-smoker	Smoker <10 cigarettes/day	Smoker ≥10 cigarettes/day
		Diabetes	Normoglycemic/ no diagnosis of diabetes	HbA1c <7.0% in patients with diabetes	HbA1c ≥7.0% in patients with diabetes

Author Man