

Exploring Early Markers of Cardiovascular Disease in Stage III Periodontitis Patients

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Background

Periodontitis is a common chronic inflammatory disease that leads to destruction of tooth- supporting tissues and contributes to systemic complications, such as cardiovascular diseases (CVD). These contributions occur via shared inflammatory pathways, modulated by CRP, IL-6, IFN- γ , and MMP-8.

Tonneti et al, *J Clin Periodontol* 2013

Hypothesis

We hypothesize that periodontitis patients with the highest levels of these markers in serum and saliva are at greater risk for CVD development.

Aim

To examine relevant clinical and demographic parameters of an established co-hort of Stage III periodontitis patients and determine levels of markers associated with cardiovascular risk.

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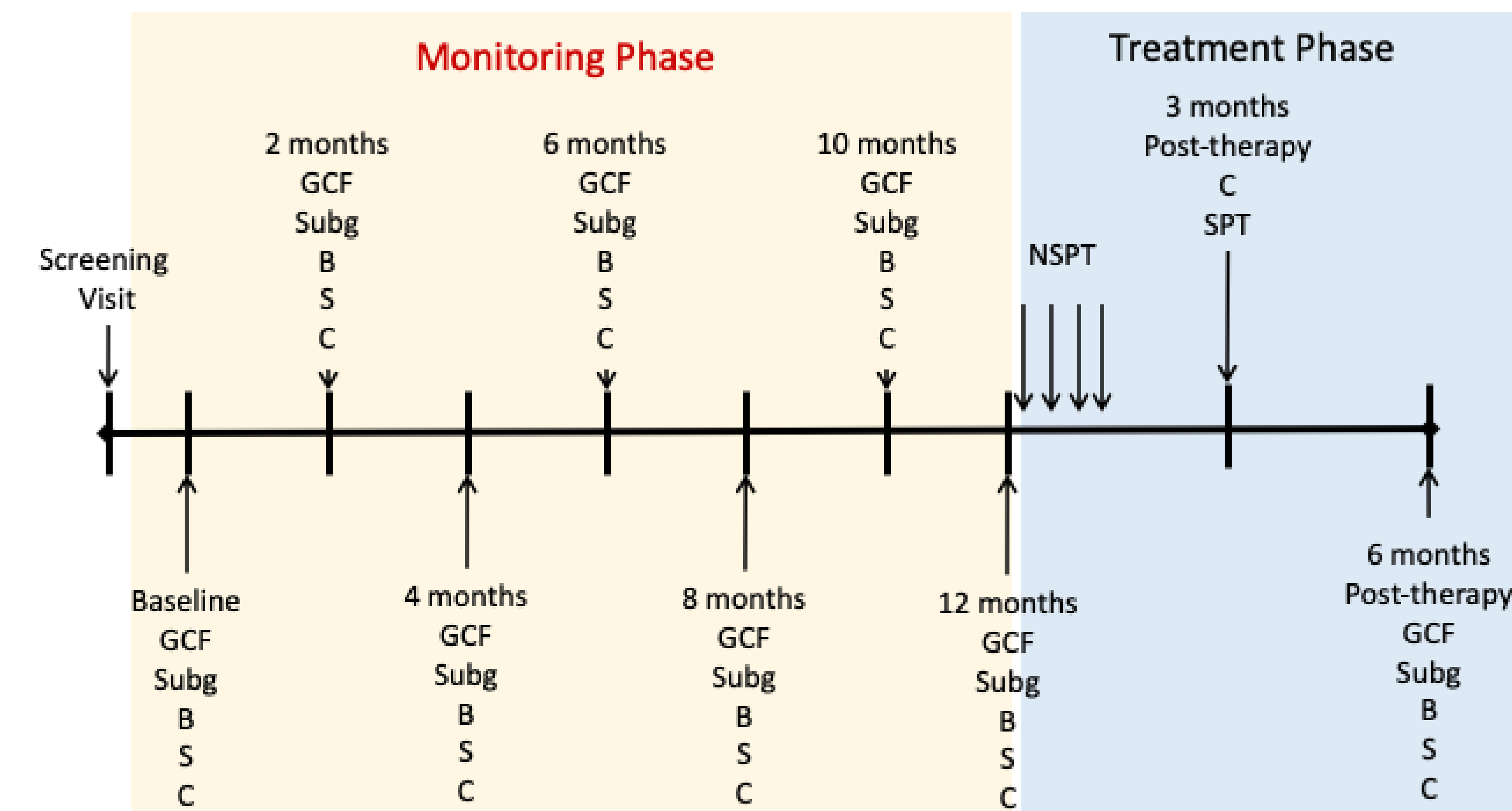
4- DMD, PhD, Professor, Department of Periodontics Director, Master of Science in Oral Biology Program, Penn Dental Medicine, University of Pennsylvania.

Methodology: Study Design and Cohort Description

Stage III Periodontitis				
Number of Subjects	268			
Progclass (P0/P1/P2)	119/101/48			
Number of Male / Female	143/125			
AA/White/Oth/Unk	78/20/13/156			
Age (years; $\mu \pm \sigma$)	51.2 \pm 11.7			
Periodontal Parameters	Baseline	12M	15M	18M
# Missing Teeth ($\mu \pm \sigma$)	1.66 \pm 1.62	1.65 \pm 1.62	1.64 \pm 1.61	1.65 \pm 1.61
PD (mm; $\mu \pm \sigma$)	2.61 \pm 1.37	2.62 \pm 1.31	2.32 \pm 1.13	2.34 \pm 1.11
CAL (mm; $\mu \pm \sigma$)	2.39 \pm 1.53	2.38 \pm 1.48	2.14 \pm 1.34	2.16 \pm 1.32
% sites per subject with:				
Plaque ($\mu \pm \sigma$)	68 \pm 22	67 \pm 26	59 \pm 27	56 \pm 28
Gingival Redness ($\mu \pm \sigma$)	58 \pm 25	61 \pm 26	48 \pm 26	46 \pm 26
BOP ($\mu \pm \sigma$)	47 \pm 24	44 \pm 24	33 \pm 22	31 \pm 20
Suppuration ($\mu \pm \sigma$)	0 \pm 4	0 \pm 2	0 \pm 3	1 \pm 3
Number of Sites / Subject				
PD < 4 mm ($\mu \pm \sigma$)	127.49 \pm 21.39	128.54 \pm 21.84	139.61 \pm 19.69	140.73 \pm 16.96
PD 4-6 mm ($\mu \pm \sigma$)	27.82 \pm 16.49	26.99 \pm 17.75	16.09 \pm 12.69	15.56 \pm 11.75
PD >6 mm ($\mu \pm \sigma$)	2.08 \pm 3.81	1.93 \pm 3.46	1.06 \pm 2.25	0.94 \pm 1.94
PD <5 mm ($\mu \pm \sigma$)	140.96 \pm 16.98	143.43 \pm 16.65	149.83 \pm 16.35	150.66 \pm 13.17
PD 5+ mm ($\mu \pm \sigma$)	16.42 \pm 13.03	14.03 \pm 13.38	6.93 \pm 8.07	6.58 \pm 7.39
Number of Sites / Subject				
CAL <4 mm ($\mu \pm \sigma$)	128.28 \pm 24.77	130.19 \pm 24.77	137.9 \pm 22.77	138.93 \pm 21.03
CAL 4-6 mm ($\mu \pm \sigma$)	26.16 \pm 18.27	24.72 \pm 19.2	17.18 \pm 15.16	16.64 \pm 14.93
CAL >6 mm ($\mu \pm \sigma$)	2.95 \pm 5.25	2.55 \pm 4.4	1.68 \pm 3.25	1.67 \pm 3.3

Exclusion Criteria:

- ✓ periodontal or systemic antibiotic therapy in the previous 6 months;
- ✓ **the use of tobacco products within 1 year** before the screening visit;
- ✓ any medical condition that might influence the course of periodontal disease or treatment;
- ✓ chronic use of NSAIDs; systemic immunosuppressive agents;



MCP1
IFN-g
IL6
VEGF
IL8
IL1-b
MMP8
IL10
OPG
MMP9

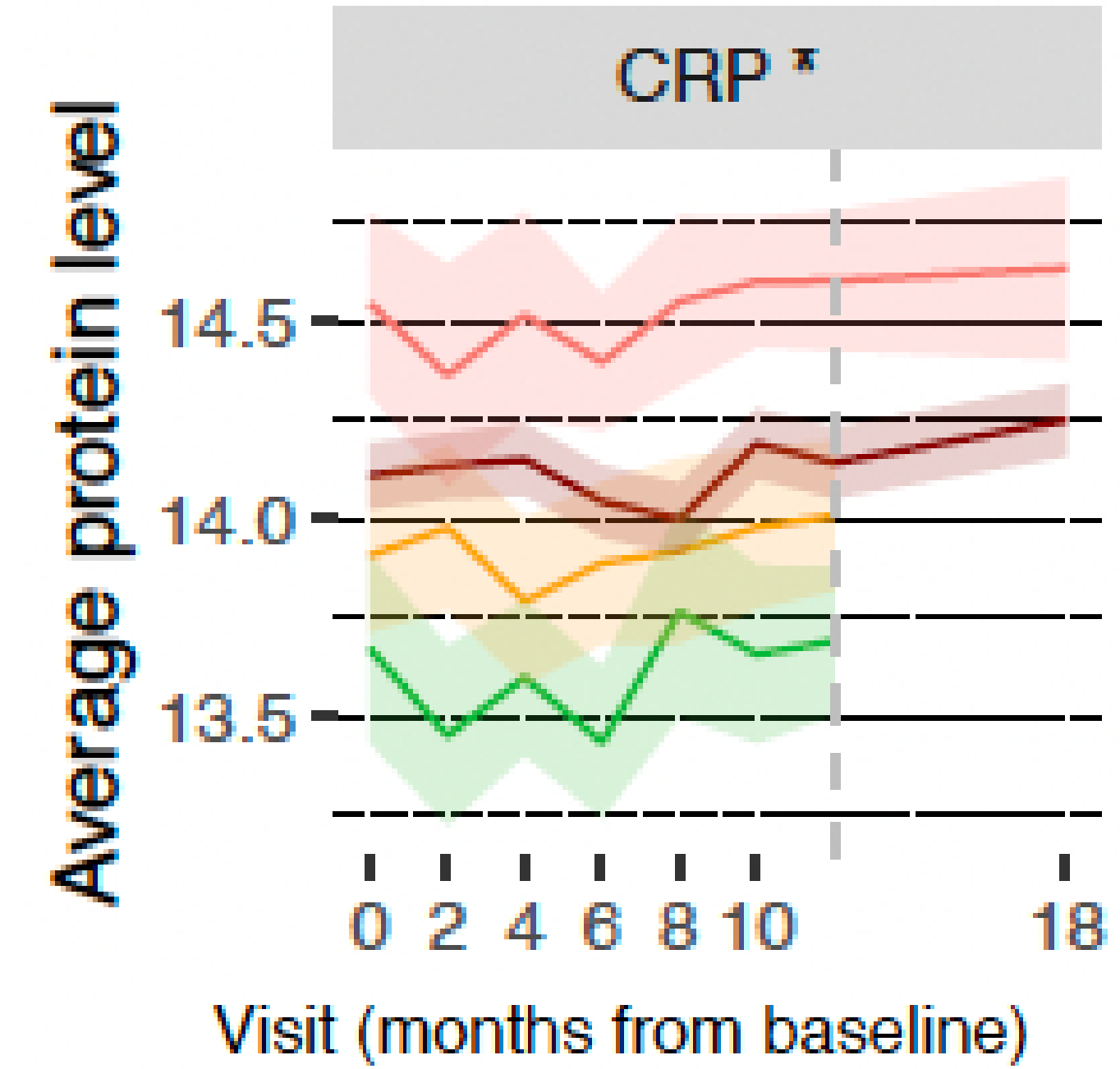


CRP
HSA
MPO
MMP8
MMP9



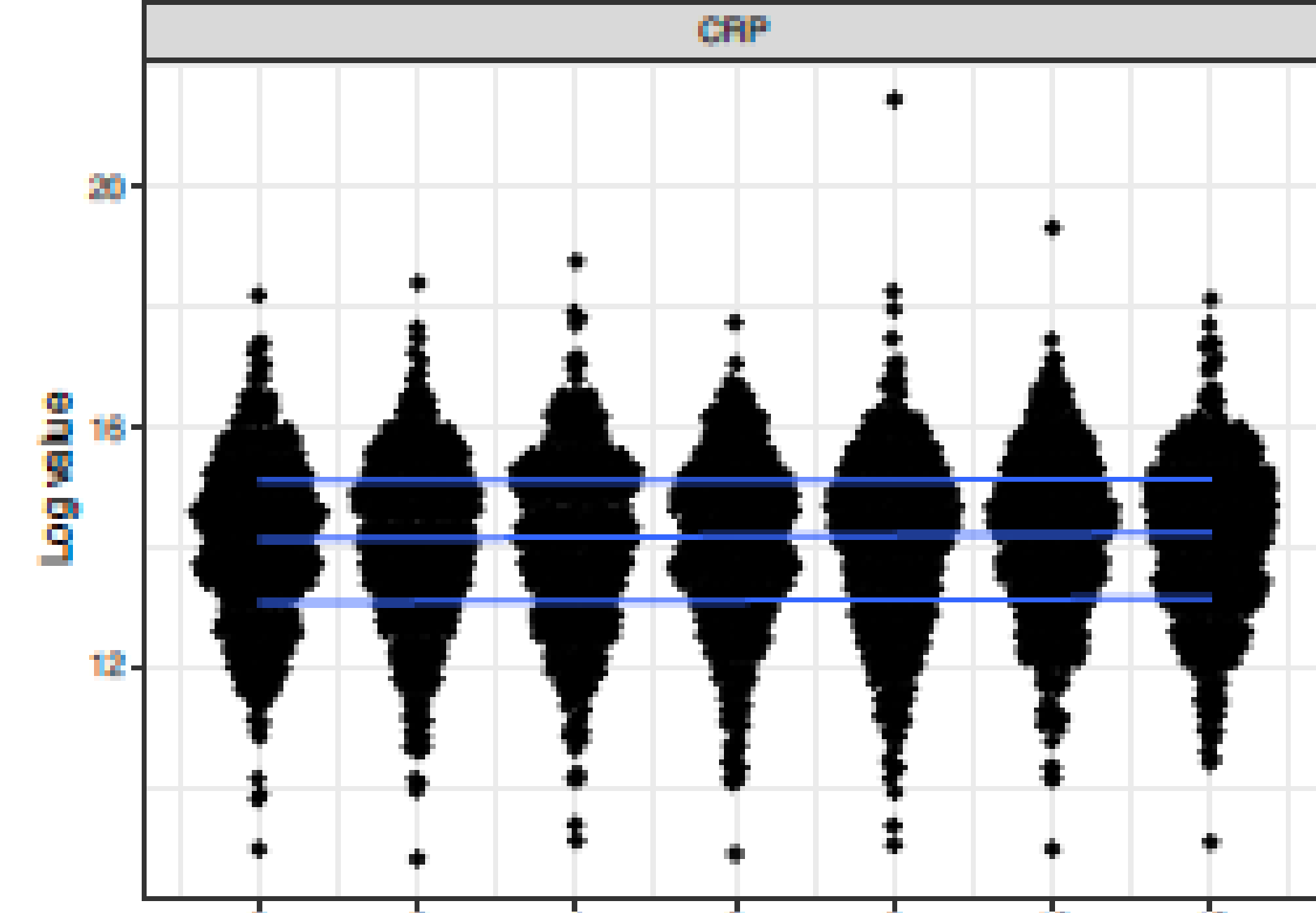
Teles et al, *J Clin Periodontol* 2018, 2024a, 2024b

Results: Characteristics of Upper and Lower Quartiles of Serum CRP



Healthy
Gingivitis
II
III

n=268



Quartiles of Log Transformed serum CRP

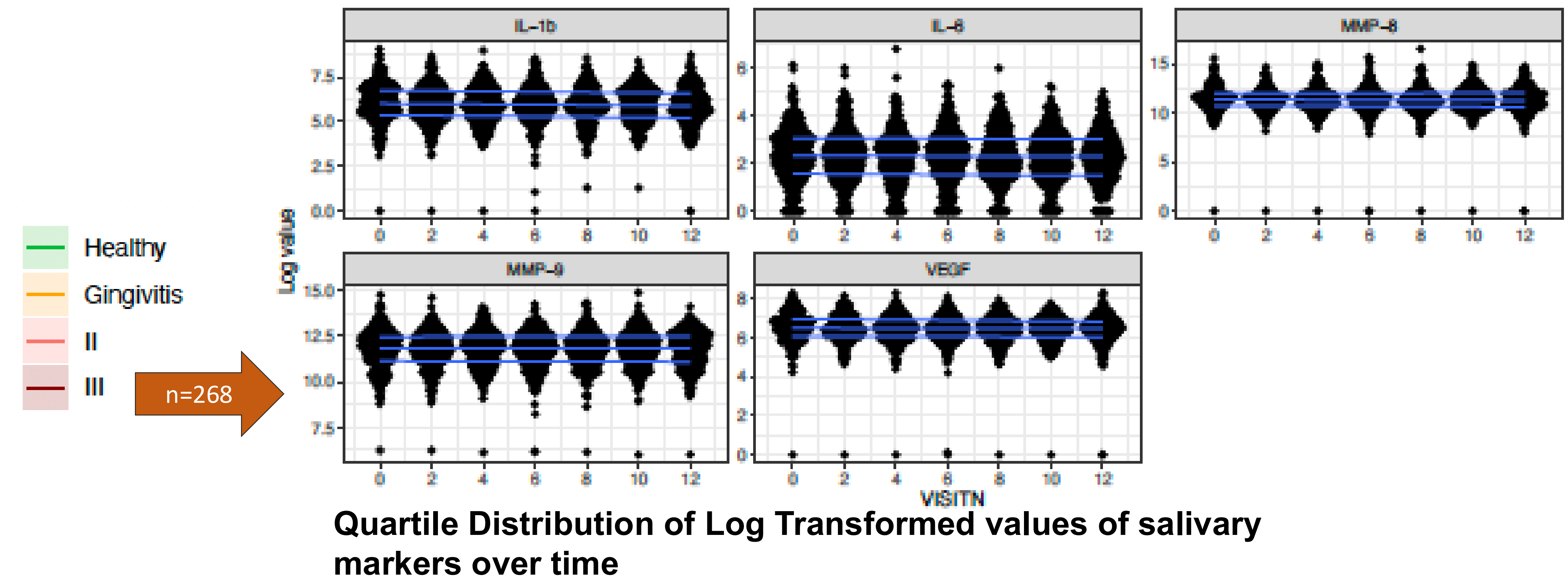
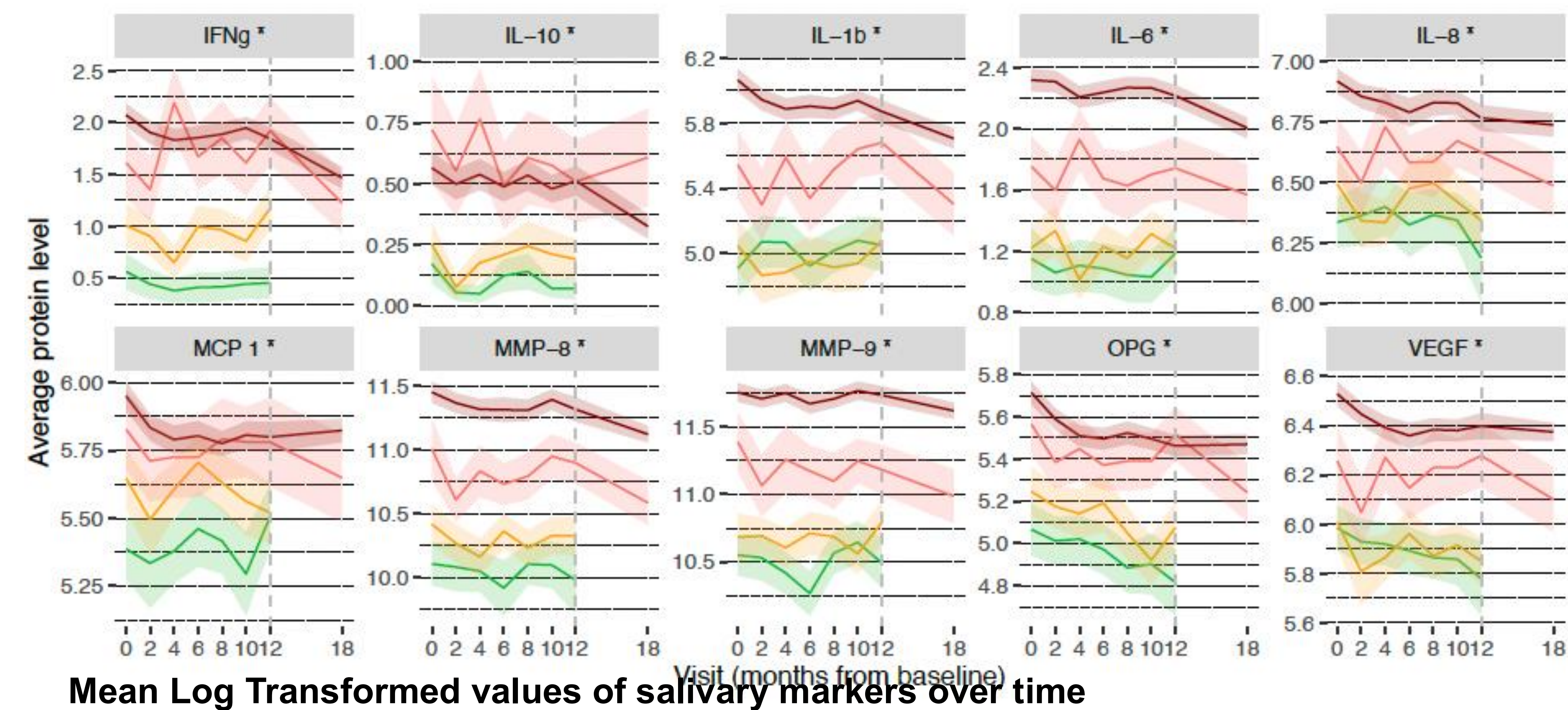
At 12 M visit	Q1		Q4	
	Mean	SD	Mean	SD
CRP (pg/mL)	278,045.01	157,198.25	11,038,998.46	12,182,726.21
CRP (Log)	12.31	0.78	15.9	0.7
Age	50	12.2	50.66	9.99
Missing Teeth	1.69	1.56	1.75	1.6

Standard cardiovascular risk interpretation (hs-CRP):		
Clinical Category	mg/L	pg/mL
Low risk	< 1 mg/L	< 1,000,000 pg/mL
Moderate risk	1–3 mg/L	1,000,000–3,000,000 pg/mL
High risk	> 3 mg/L	> 3,000,000 pg/mL
Acute inflammation	> 10 mg/L	> 10,000,000 pg/mL

Characteristics of Lower and Upper Quartiles of Serum CRP at 12M

category	Variable	Q1	Q4
SEX	Female	34	38
	Male	31	27
ETHN	Hispanic or Latino	10	8
	Not Hispanic or Latino	55	57
RACE	American Indian/Alaska Native	NA	1
	Asian	6	NA
	Black or African American	15	27
	More Than One Race	NA	1
	Unknown or Not Reported	3	3
Mean Number of Sites	Bleeding on Probing	40.8 ± 2.8	42.7 ± 2.5
	Gingival redness	55 ± 0.2	58 ± 0.2
	PD (mm)	2.53 ± 0.004	2.58 ± 0.004
	PDEPM < 4	131.1	124
	PDEPM < 5	143.7	141
	PDEPM > 6	4.5	4
	PDEPM > 4 & PDEPM < 6	13.3	16.1
	PDEPM > 5	8.3	8.2
	CALM < 4	127.5	127
	CALM > 4 & CALM < 6	14.2	12.5
	CALM > 6	5.8	4.6

Results: Characteristics of Upper and Lower Quartiles of Salivary Markers



Clinical Characteristics of Upper and Lower Quartiles of Salivary Markers

Visit : 12M		Q1	Q4	Q1	Q4	Q1	Q4	Q1	Q4	Q1	Q4
Salivary Marker		IL-6		MMP-8		MMP-9		IL-1b		VEGF	
Number of Sites:	PDEPM < 4	139.1	117.4	137.6	119.9	136.0	117.2	136.1	120.2	134.8	122.9
	PDEPM < 5	149.4	136.7	147.9	138.2	146.7	135.8	147.7	138.2	147.1	140.2
	PDEPM > 6	2.9	5.1	3.4	5.7	5.5	5.3	3.9	5.0	3.0	5.1
	PDEPM > 4 & PDEPM < 6	10.7	19.2	11.9	17.1	11.7	18.4	11.9	16.2	11.9	16.3
	PDEPM > 5	5.3	11.1	6.3	10.3	8.3	10.5	6.6	10.5	5.7	8.6
	CALM < 4	138.1	119.9	136.5	121.5	135.9	118.9	138.6	123.2	136.2	124.2
	CALM > 4 & CALM < 6	10.3	17.3	12.0	14.4	11.5	16.2	10.3	14.4	10.4	14.6
	CALM > 6	3.9	5.5	4.4	6.8	6.3	5.8	4.6	5.4	5.3	5.7
	% Sites Progressing	2.1	3.3	2.7	3.0	3.4	2.4	2.1	3.2	2.1	2.8

Conclusion and Next Steps

- Higher levels of both salivary and serum inflammatory markers are associated with older age, more extensive gingival redness and bleeding on probing as well as greater mean pocket depth and progressive loss of attachment.
- Exploring the presence of cardiovascular specific proteins in those patients may improve the assessment of their risk for cardiovascular disease
- Current work is extending these findings by including CVD markers indicative of cardiovascular stress.

