

Oral Microbiome and Systemic Health

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Genomic Medicine IV

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**Support:
MCRF, Delta Dental, ICTR
NHGRI (Ian Marpuri)**



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Oral Microbiome and Systemic Health Research Project

Goal: to establish an Oral/Systemic Health Cohort for research across multiple institutions

Process: standardized enrollment of patients with EHR and EDR, standardized clinical tests, standardized microbiome characterization, genomic DNA, plasma and serum to advance Translational Medicine and Dental Care

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Mount Sinai School of Medicine

Morehouse School of Medicine

University of Pittsburgh

University of Pennsylvania

Ohio State University Medical Center

University of North Carolina

University of Medicine and Dentistry of New Jersey

University of Illinois at Chicago

Cleveland Clinic

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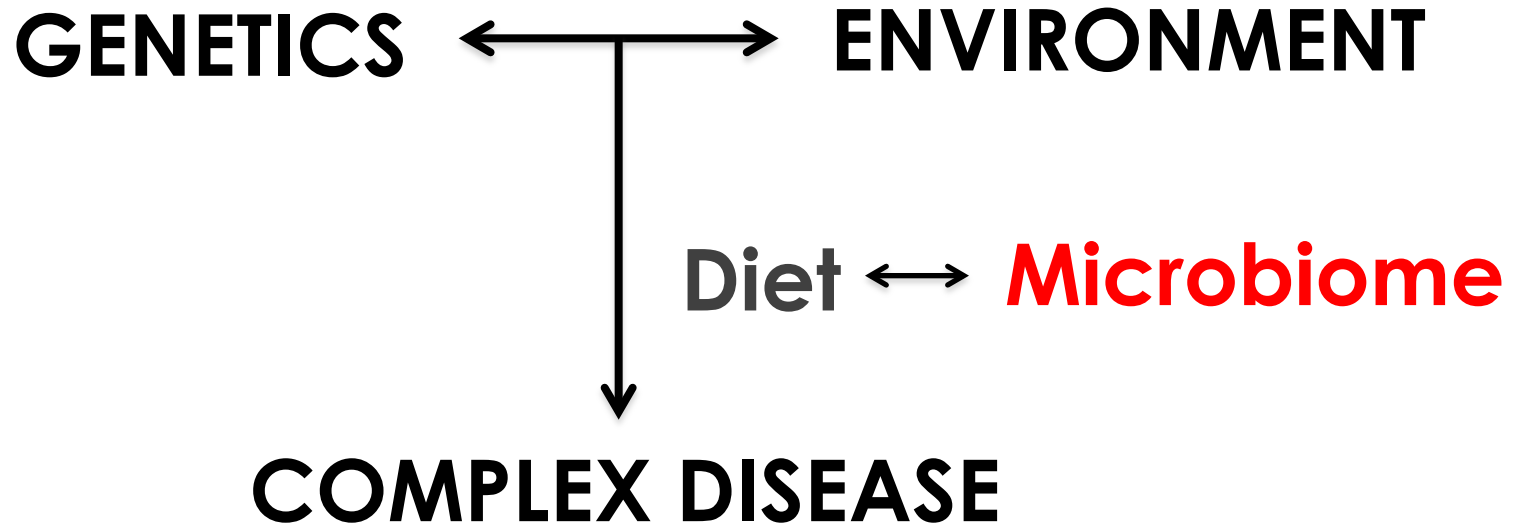
Spoiler Alert

- The mouth is part of the body
- The microbiome needs to be factored in for risk assessment for some of the most common and costly diseases
- Microbiome must be part of Personalized Medicine
- A consortium of patient cohorts with standardized recruitment, sample collection and data will advance the field

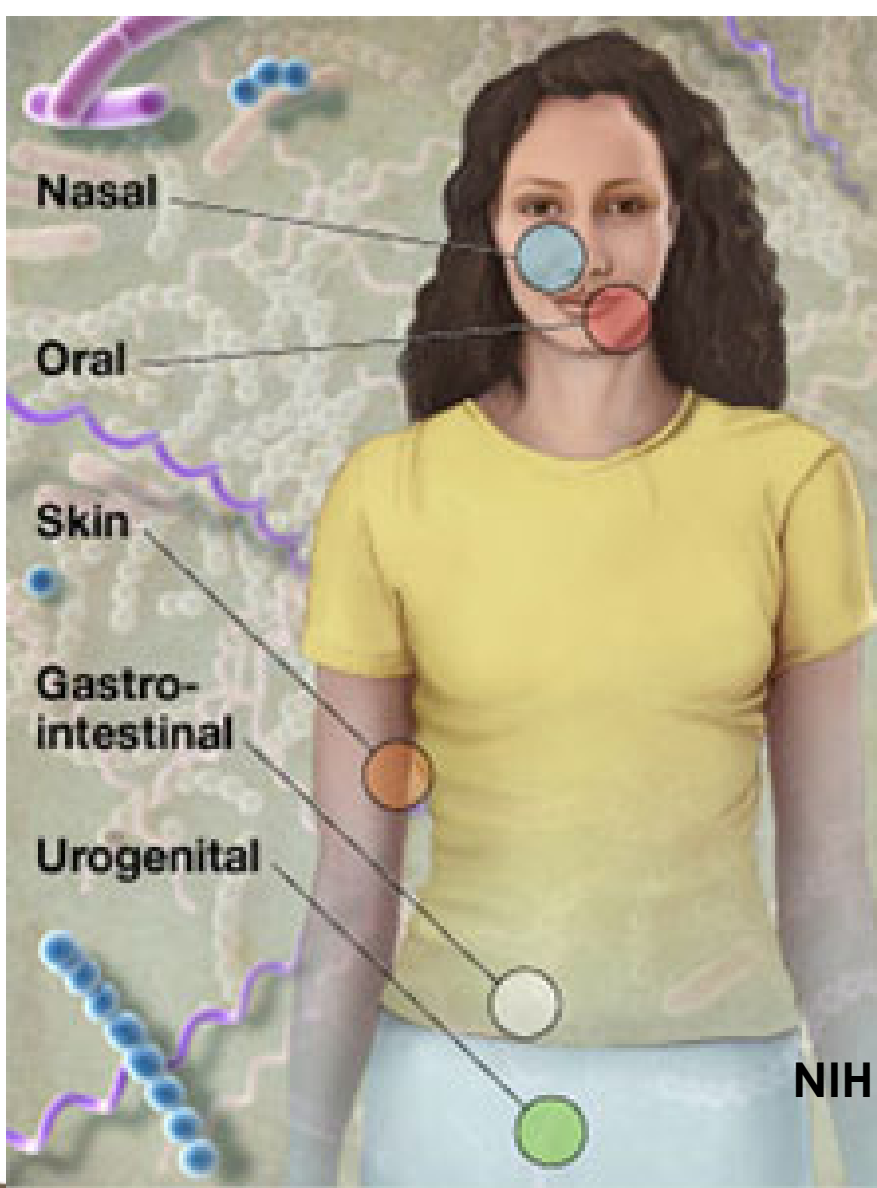


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T2D, RA, CAD
Enhance prediction
health disparities



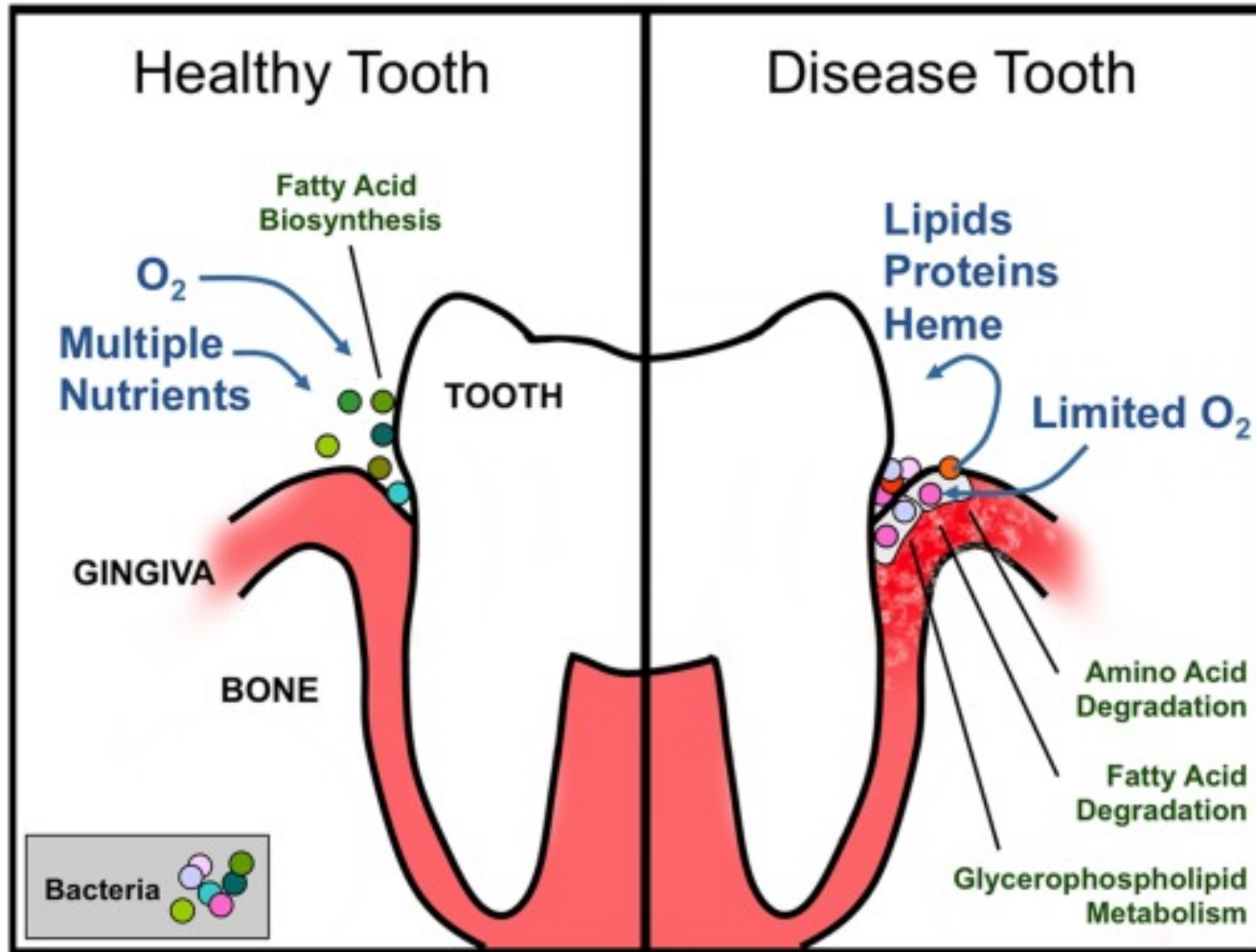
NIH Human Microbiome Project



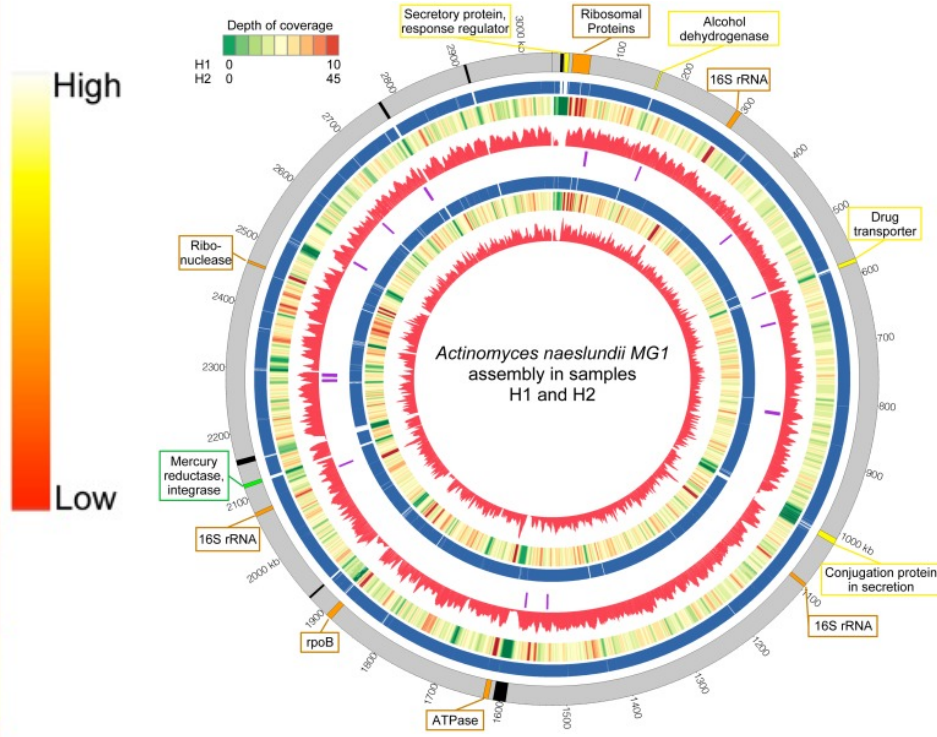
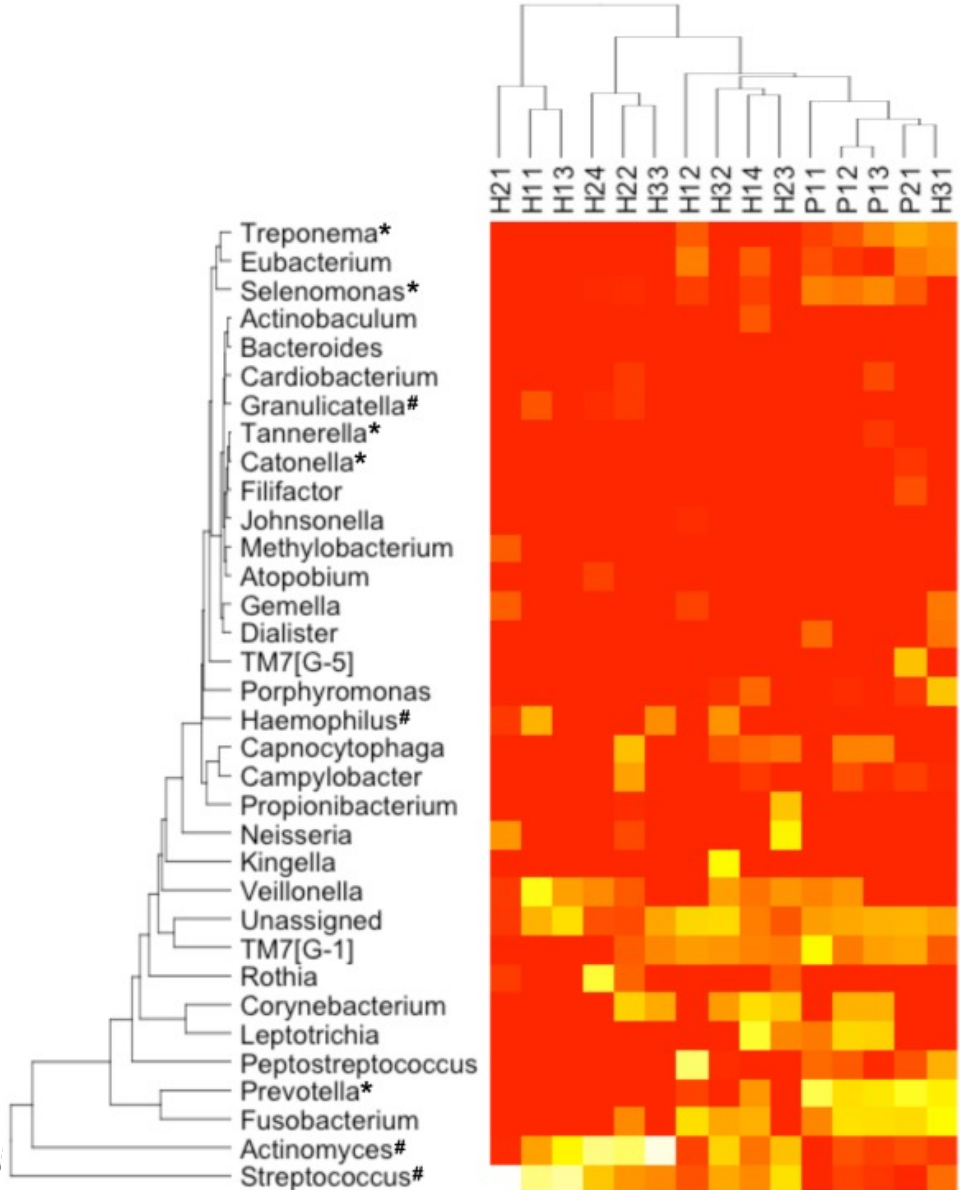
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Deep Sequencing of the Oral Microbiome Reveals Signatures of Periodontal Disease, Liu et al, PLoS One. 2012; 7(6): e37919



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Oral Systemic Health Research Project

Progress to date:

- Series of conference calls to plan the initiative
- Organizing National Oral Systemic Health Consortium with standardized recruitment criteria
- Phase I (Pilot Project) completed at Marshfield
- Standardized recruitment
- Standardized sample collection
- Standardized questionnaire
- 41 patients enrolled – added to PMRP cohort
- Published manuscript outlining the project
- Planned enrollment of (Phase II) 2,000 additional subjects at Marshfield Clinic
- **Planned enrollment of 400 subjects at Mt. Sinai**



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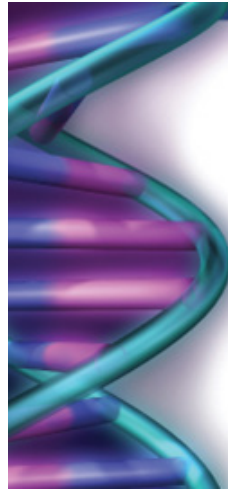
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Oral Systemic Health Research Project

Long term
EMR Data



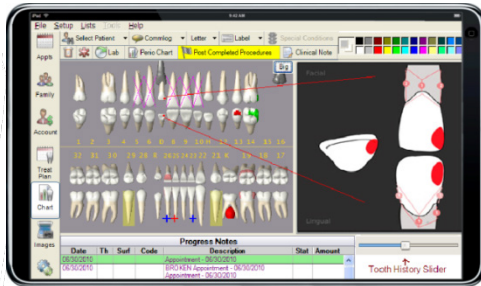
Host DNA Data



Oral Microbiome Data



EDR Data



Plasma & Serum Samples



Standard Clinical Tests
at enrollment



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- **Inclusion/Exclusion criteria**
- **Periodontitis case definition**
- **Types of oral samples to be collected**
- **Number of oral samples to be collected per patient**
- **Timing of collection of samples**
- **Ability to follow-up patient after initial sample collection**
- **Method for collection of oral samples**
- **Method for extraction of nucleic acids from oral microbiome samples**
- **Method for identifying microbial species present in the oral samples**
- **Methods for other 'omics**
- **Other types of biological samples to be collected**
- **Other primary phenotypes of interest**



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INVITED MEDICAL REVIEW

The oral-systemic personalized medicine model at Marshfield Clinic

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Periodontal disease and diabetes, two diseases that have achieved epidemic status, share a bidirectional relationship driven by micro-inflammatory processes. The present review frames the current understanding of the pathological processes that appear to link these diseases and advances the hypothesis that reversal of the epidemic is possible through application of interdisciplinary intervention and advancement of oral-systemic personalized medicine. An overview of how Marshfield Clinic's unique clinical, informatics and bio-repository resources and infrastructures are being aligned to advance oral-systemic personalized medicine is presented as an interventional model with the potential to reverse the epidemic trends seen for these two chronic diseases over the past several decades. The overall vision is to engineer a transformational shift in paradigm from 'personalized medicine' to 'personalized health'.

However, existing attempts at epidemiological prevalence projections support Satcher's characterization, with estimates of 75% of the US population affected by gingivitis, 35% of adults affected by periodontal disease (PD), and approximately 13% afflicted by severe periodontitis, with persons of low socioeconomic status disproportionately affected (Albandar *et al*, 1999). Emerging evidence that PD impacts exacerbation of other pathological conditions systemically has heightened concern over the high prevalence of oral disease. Of highest concern was mounting evidence demonstrating that diabetes mellitus (DM), another escalating epidemic, and PD represented reciprocal risk and exacerbation factors for each other, presumably mediated by chronic inflammatory pathophysiological mechanisms (Mealey *et al*, 2006). However, a critically important finding of some studies was that, with appropriate oral prophylaxis and intervention, exacerbation of both conditions could

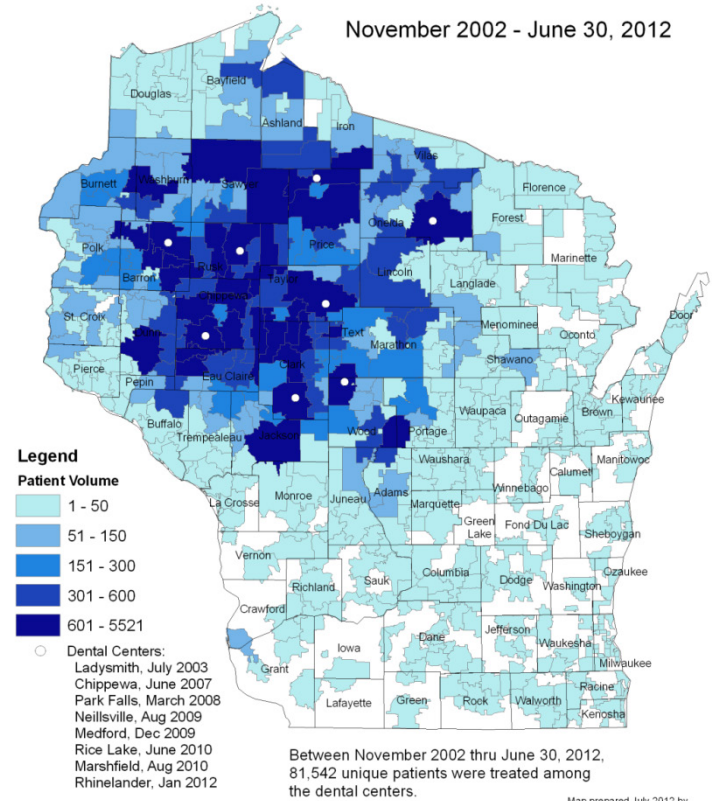
2012*

No. Dental Centers	9
Square Feet	114,181
Total Operatories	182
Training Operatories	24
Dental Students	0
Dentists (includes general dentists, oral surgeons, and a pediatric dentist)	52
Total FTEs	300.18

*includes Black River Falls clinic, opening this year

Unique Dental Patients by Zip Code Marshfield Clinic/Family Health Center - Dental Centers

November 2002 - June 30, 2012



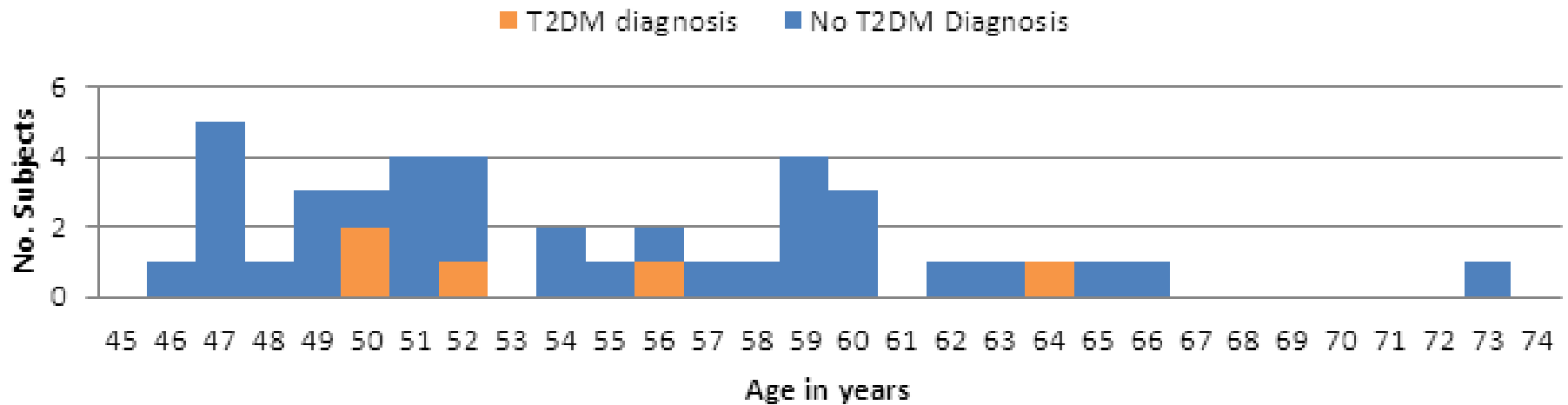
Pilot: Clinical Results to Date

Cut off value for notification	No. subjects at visit 1 n=41
Cholesterol >200	16
Fasting blood glucose >100	14
Microalbumin >1	11
ave left systolic BP >140	4
ave right systolic BP >140	4
ave left diastolic BP >90	2
ave right diastolic BP >90	4
hs-CRP >3	16
HbA1c >7	0
TOTAL	71

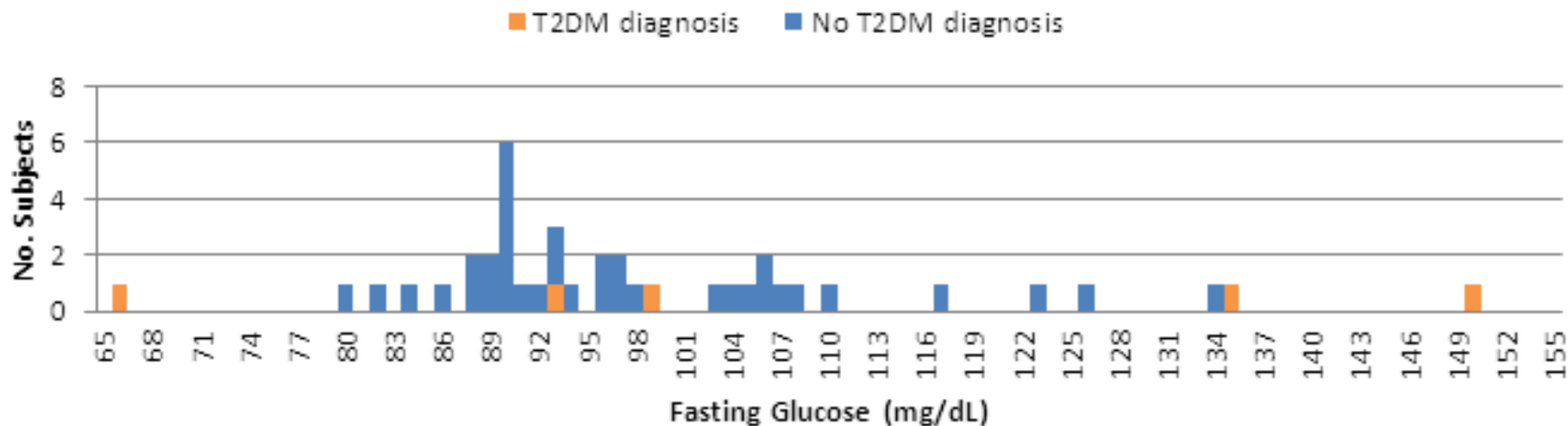
No. lab values per person triggering notification	No. subjects at visit 1 n=41
1 value	11
2 values	16
3 values	5
4 values	2
5 values	1
TOTAL	35



Age and T2 Diabetes Distribution of OSRP Pilot Subjects at Enrollment (n=41)



Fasting Glucose and T2 Diabetes Distribution of OSRP Pilot Subjects at Enrollment (n=41)

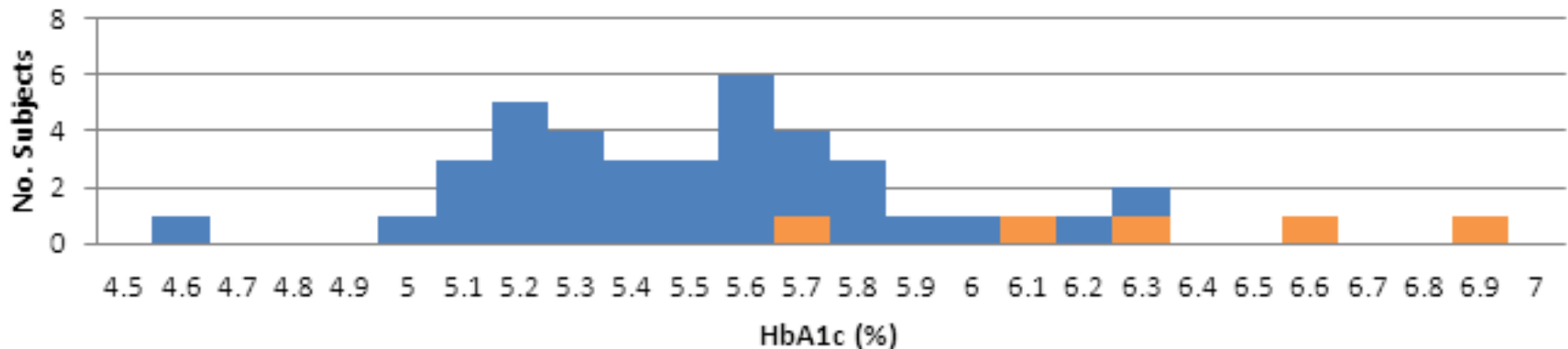


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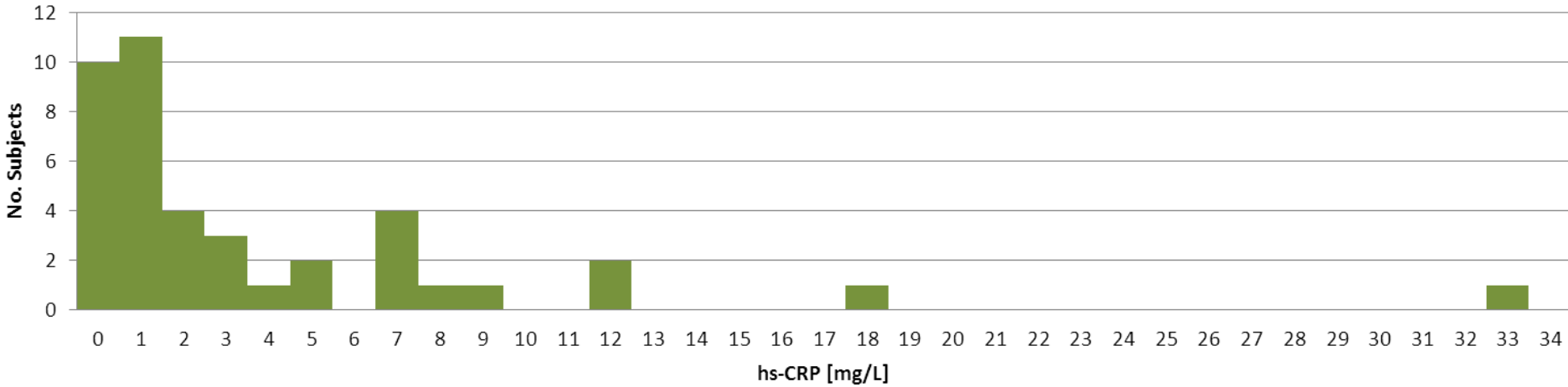
HbA1c and T2 Diabetes Distribution of OSRP Pilot Subjects at Enrollment (n=41)

■ T2DM diagnosis ■ No T2DM diagnosis



C reactive Protein results

High Sensitivity C-Reactive Protein Distribution of OSRP Pilot Subjects at Enrollment (n=41)



hs-CRP	cardiovascular risk	no. subjects	% subjects
<1	low risk	10	24.39
1-3	average risk	15	36.59
>3	high risk	16	39.02

We will continue efforts to form a network of like-minded institutions across the country to establish a large and diverse cohort of dental/medical patients with EHRs, EDRs and oral microbiome samples.

In addition to T2D, RA and CAD, this cohort can be used to implement PGx in dentistry, including pain control and coagulation management.

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- MFLD Clinic laboratory staff

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Dental clinics' staff

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