Periodontal Diseases: Effects on Diabetes Control and Complications

Clinical Directors Network-Community Health Centers-University of Michigan School of Dentistry Collaboration
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Overview

◆ Overview of diabetes and periodontal diseases

◆ Conceptual model of chronic periodontal inflammation and insulin resistance

◆ Periodontal infection and insulin resistance: empirical evidence

◆ Periodontal infection and glycemic control: empirical evidence

  ◆ Observational studies
  ◆ Treatment studies

◆ Significance of improving glycemic control

◆ Periodontitis and complications of diabetes

◆ Current collaboration with CDN and CHC's

Diabetes Mellitus

| Type 1 5-10% | Type 2 90-95% | Gestational 2-5% | Other 1-2% |

Insulin: action, production, or both

Hyperglycemia and other and metabolic abnormalities

Chronic Complications

Atherosclerosis	Neuropathy
Retinopathy	Perio diseases
Nephropathy	Impaired wound healing

Diabetes Overview

- Prevalence: 20.8 mil; 7.0% of U.S. pop.
  - Diagnosed: 14.6 mil
  - Undiagnosed: 6.2 mil
- Incidence: 1,300,000 /yr
- Prevalence by age
  - 60+: 20.9%
  - 20+: 9.6%
  - <20: 0.22%

Diabetes Overview (con't.)

- Prevalence by race/ethnicity (20 yrs+)
  - Non-Hispanic whites: 8.7%
  - Non-Hispanic blacks: 13.3%
  - Hispanic/Latino Americans: 9.5%
  - Native Amer. and Alaska Natives: 15.1%
  - Asian Amer. & Pacific Islanders: up to 2.5x nHwhite

http://www.cdc.gov/diabetes/pubs/estimates05.htm#fig2, Feb, 2006

Age-Standardized Prevalence of Diagnosed Diabetes per 100 Adult Population, by State, United States

1994

2003

Legend: < 4% | 4 – 4.9% | 5 – 5.9% | 6+ %
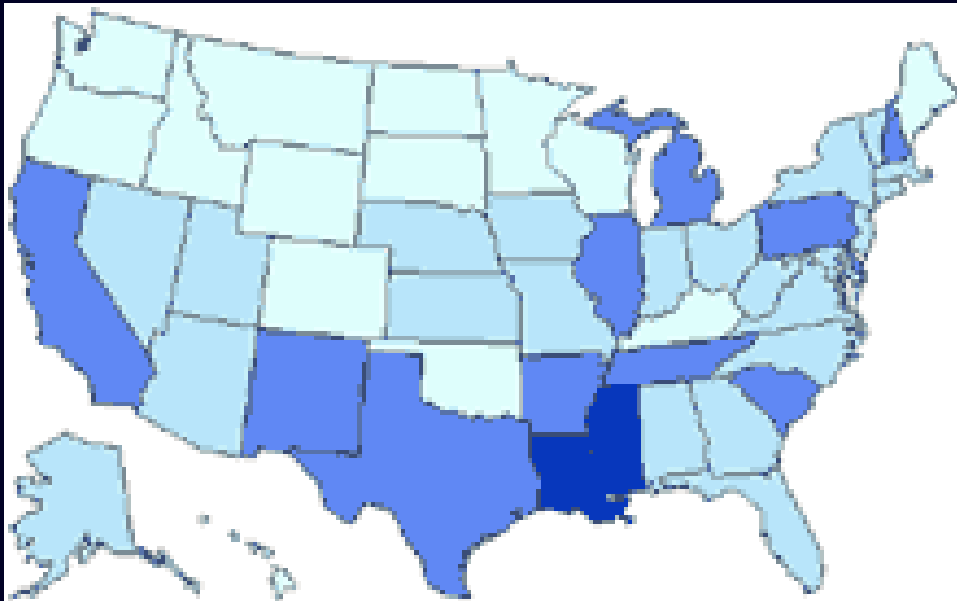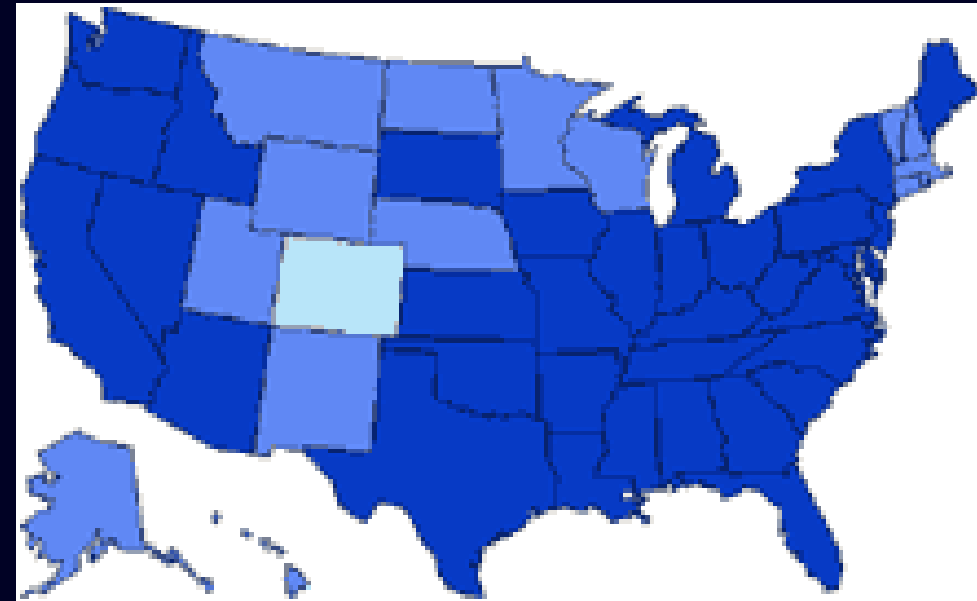
What is periodontal disease?

Periodontal disease

- Chronic inflammatory disease
- Bacterial etiology
  - Gram negative anaerobes are prominent
- Destruction of periodontal tissues
  - Formation of pathologic pockets around teeth
  - Loss of connective tissue attachment
  - Loss of alveolar bone
- Can lead to tooth loss

Gingivitis

- Bacterial plaque
- Initial periodontal disease
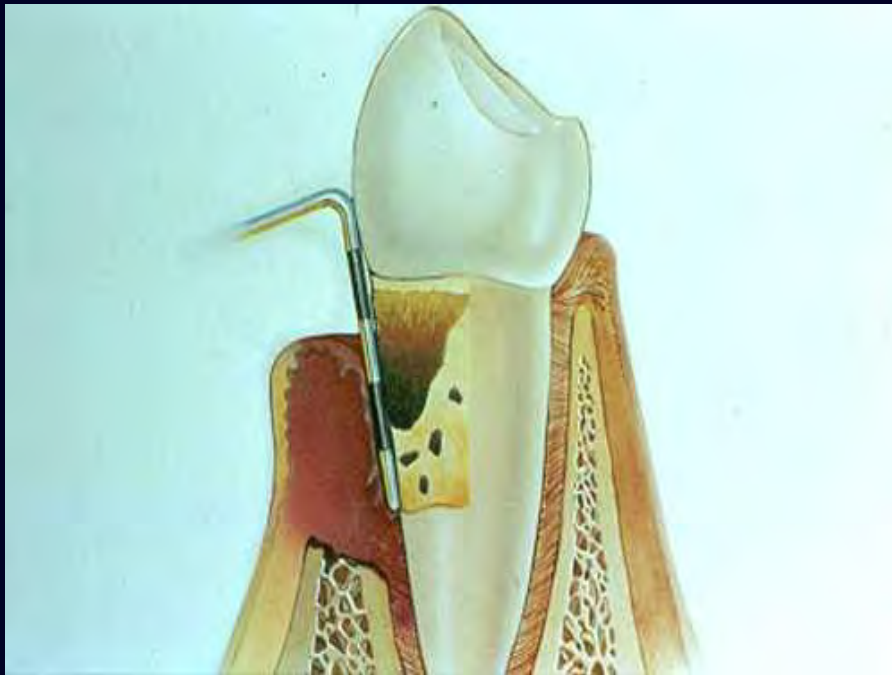- Inflamed gingiva
- Reversible
- Can progress if untreated

Periodontitis

- Bacterial plaque
- Advanced periodontal disease
- Connective tissue loss
- Periodontal ligament loss
- Supporting bone loss

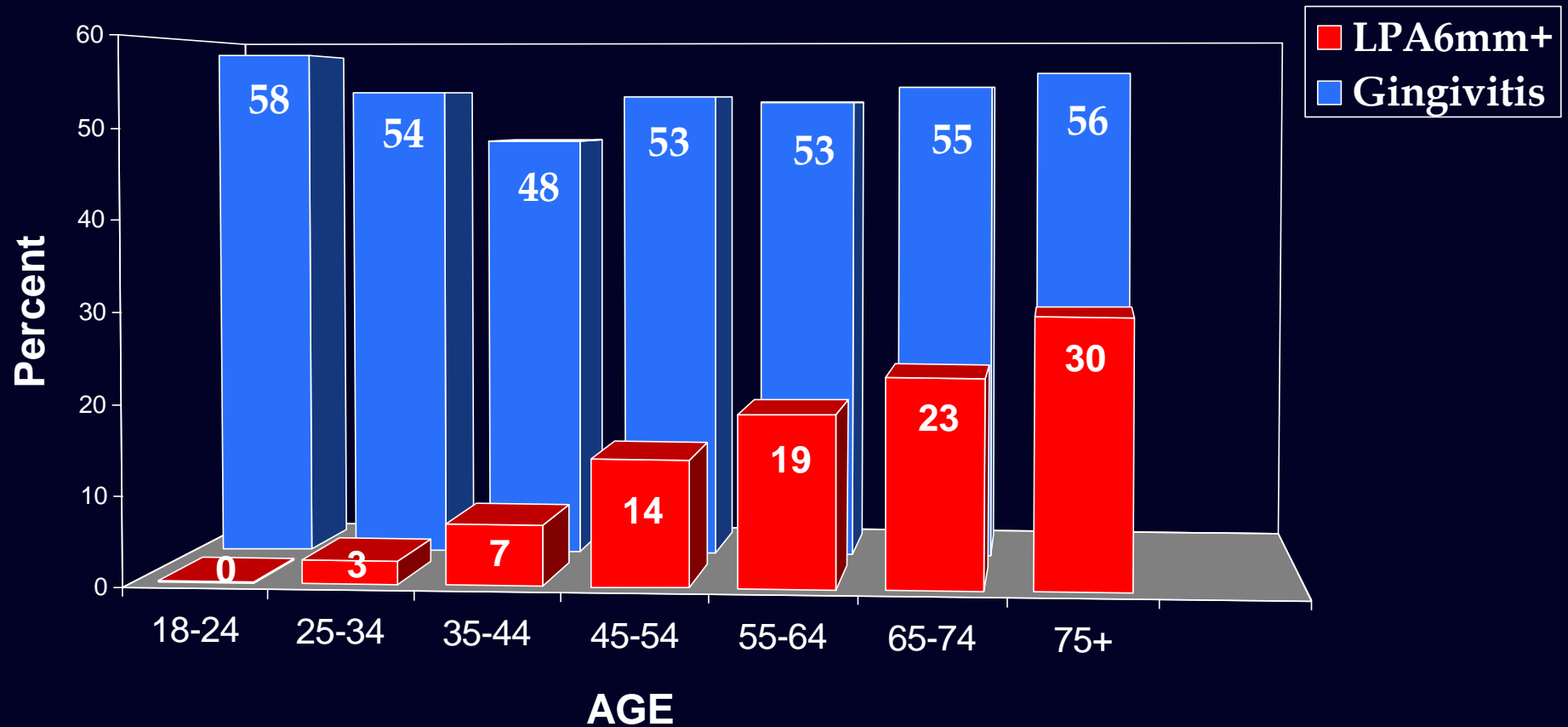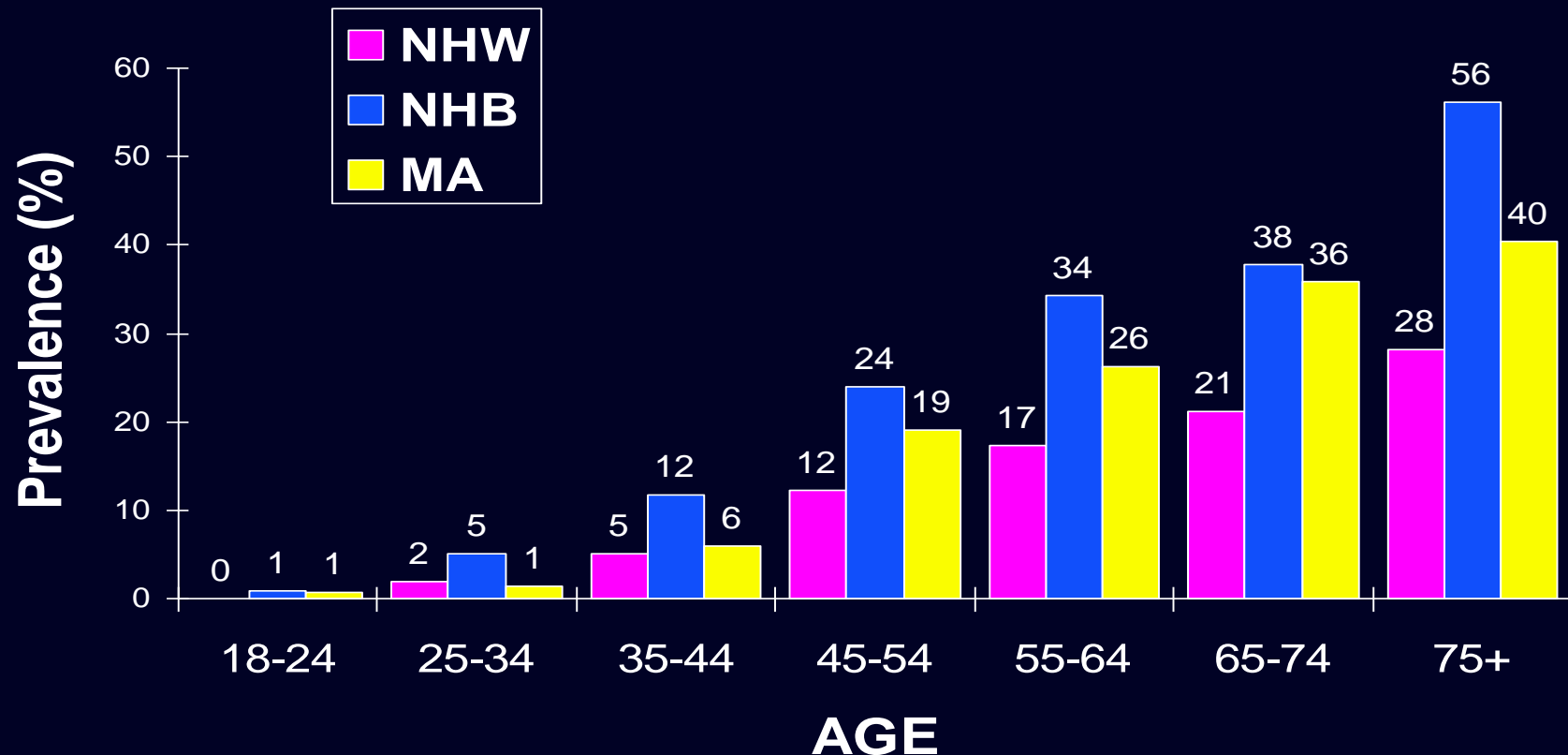# *Measuring periodontal status*

Clinical

Radiographic

How prevalent is periodontal disase?

Gingivitis and severe periodontal disease prevalence (1+ sites with LPA 6+ mm)

Source: NHANES 3 (1989-94), US Population

Severe Periodontitis by race/ethnicity: U.S. population (attachment loss > 6mm)

Source: NHANES III (1989-94), US Population

Diabetes and periodontal health
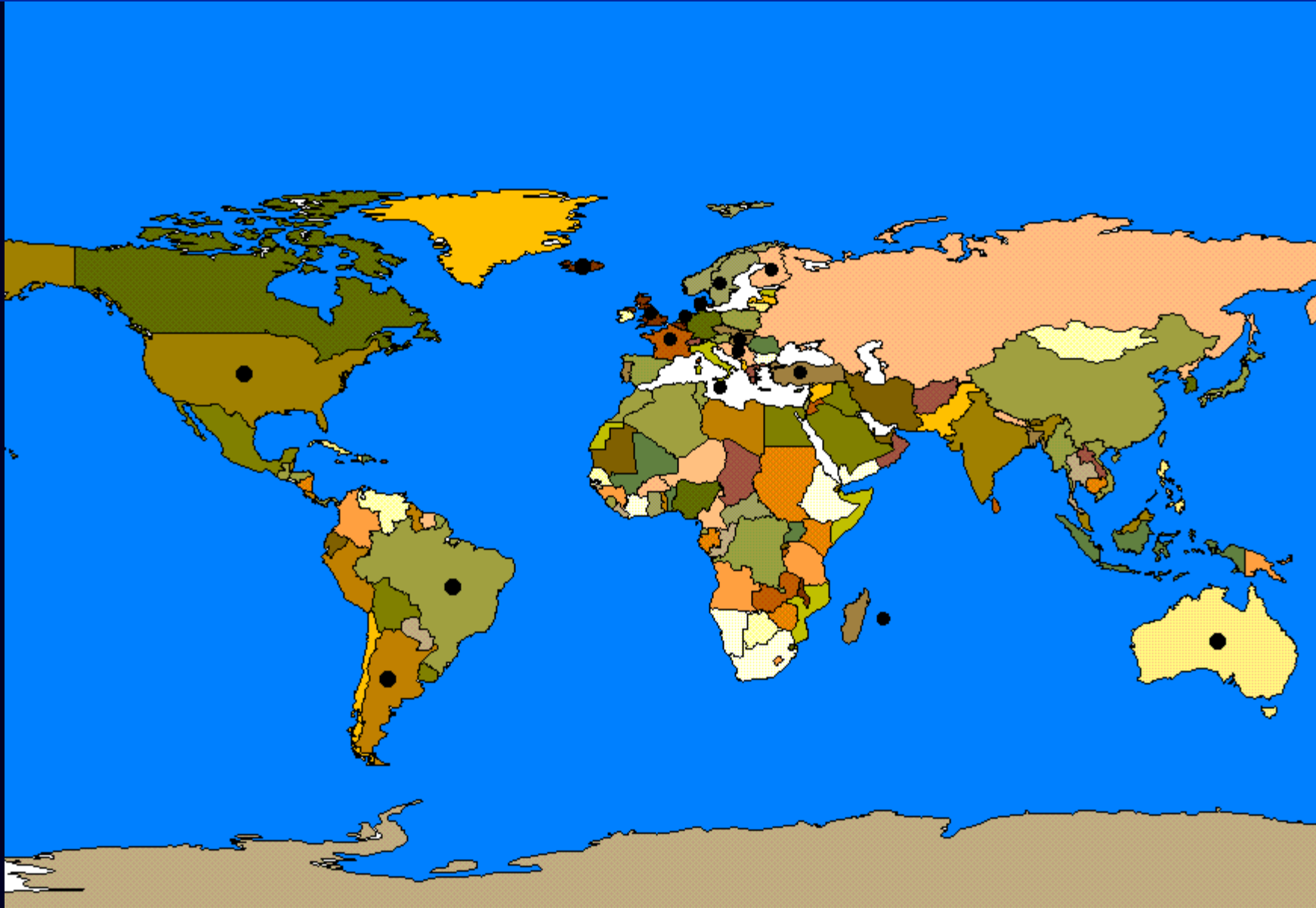
%Children and adolescents with 1+ sites with periodontal attachment loss ≥ 2mm. (Lalla E et al. 2006)
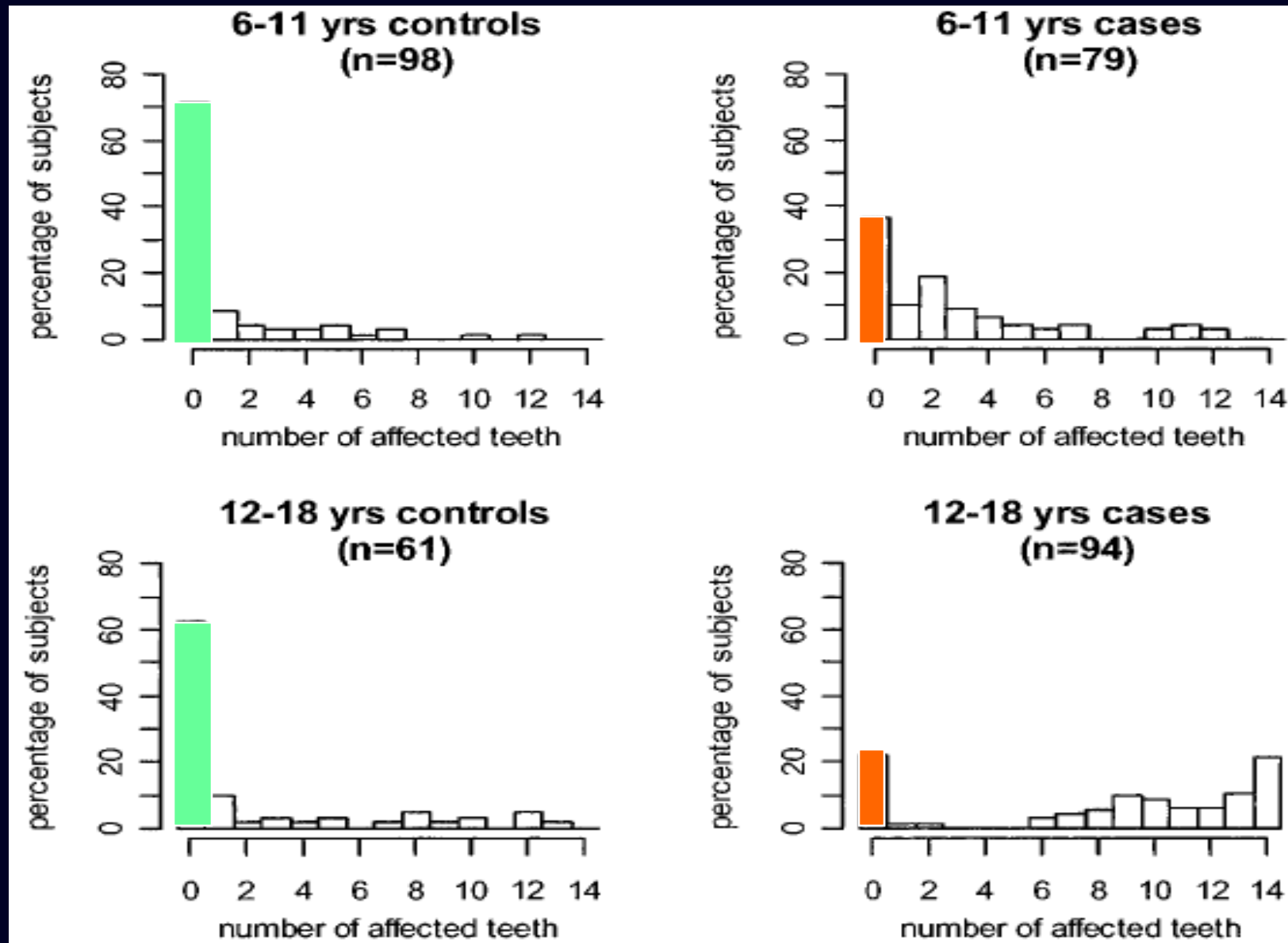
Incidence of Alveolar Bone Loss after ~2 yrs Follow-up in the Pima Indians

Legend:
- NoDM: n=338
- HbA1 < 9%: n=14
- HbA1 9%+ : n=7

None: 60, 43, 14
Some: 41, 57, 86
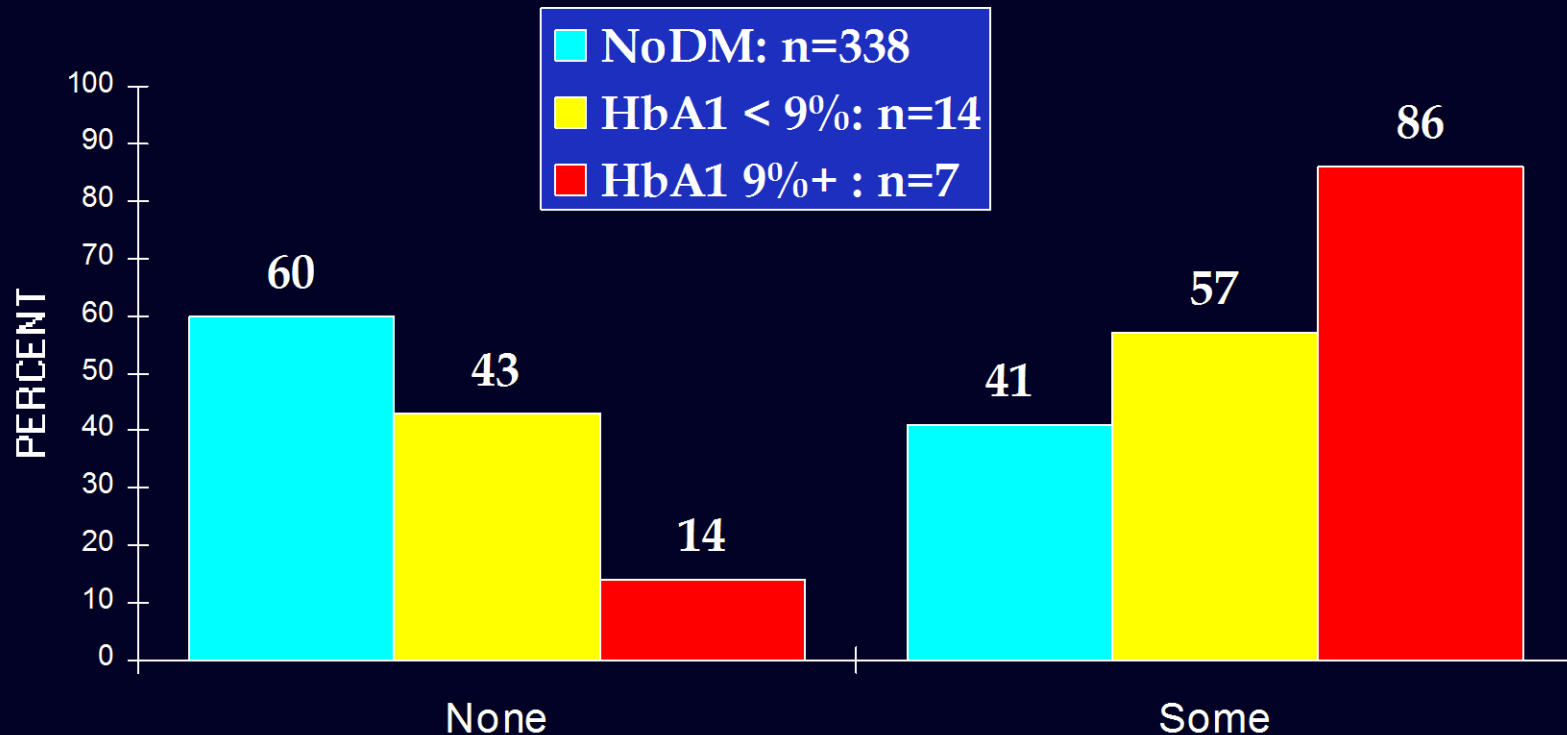
Source: Taylor et al., 1998

Why do we think periodontal disease can have an adverse effect on glycemic control?

Periodontitis and Chronic Systemic Inflammation

Relationship to Insulin Resistance

Response to Bacterial Plaque in Disease

Fatty acids
FMLP
LPS

IL-8

Low
IL-10
TGF-b
IL-1ra
TIMPs

High
TNFα
IL-6
IL-1β
IFN-g
PGE2
MMPs
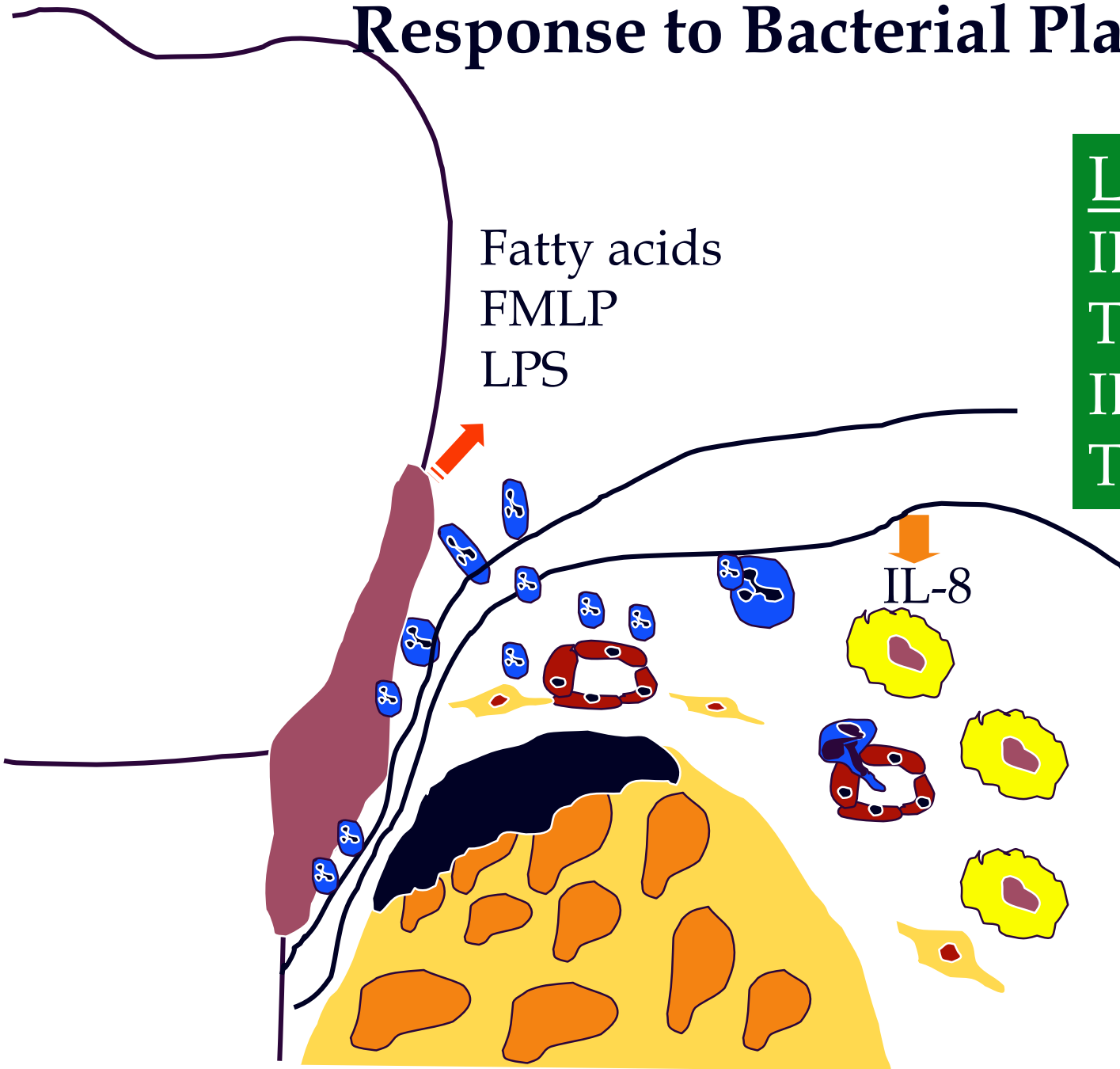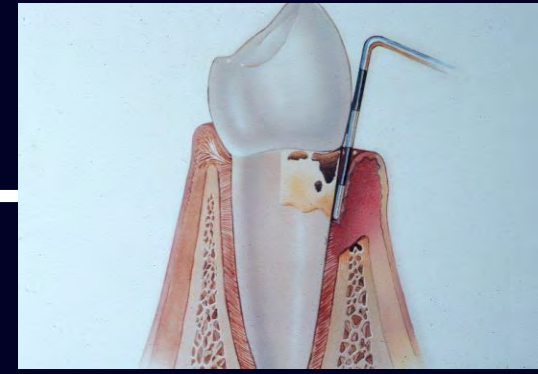
Chronic inflammation
Visceral obesity

Il-6

TNFα

Proinflammatory state
Chronic overexpression of cytokines

Pancreatic beta cell damage

Liver

Insulin resistance

Acute Phase Response (CRP, Fibrinog., PAI-1)

Glycemic Control

Conceptual Model: From Richard Donahue, 2004

What empirical evidence do we have to link periodontal disease to insulin resistance and glycemic control?

Supporting epidemiologic evidence: cross-sectional and longitudinal studies

- ◆ Inflammation and insulin resistance

- ◆ Insulin resistance and diabetes

- ◆ Inflammation and diabetes

- ◆ Periodontitis and the acute-phase response

Periodontitis and Insulin Resistance: Epidemiologic Evidence of an Association

Periodontitis and Insulin Resistance in U. S. Adults, NHANES III, Preliminary Results

◆ To evaluate the association between severe periodontitis and insulin resistance in a representative sample of U.S. adults, ages 17-90 years old.

MAJOR EXPOSURE

◆ **Severe periodontitis**

◆ At least 1 site with 6 mm or more of attachment loss

&

◆ Gingival bleeding at the teeth with 6+ mm of attachment loss

OUTCOME

◆ **Insulin Resistance**

HOMA formula

Fasting insulin (FI)
Fasting glucose (FG)

$$\frac{FI \times FG}{22.5}$$

Dichotomous variable using the 80th percentile as the cutpoint

Association between severe periodontitis and insulin resistance (HOMA 80th): crude odds ratio

- Total study group: N=5313 individuals

- Severe periodontitis: n=281 (5.3%)

- Insulin resistance
  - No severe periodontitis: n=1474 (24.6%)
  - Severe periodontitis: n=100   (38.7%)

- ASSOCIATION: Crude Odds Ratio: 2.3 (1.58, 3.39)

Logistic regression model
Response: HOMA 80th (n=1574/5313)

COVARIATE	OR	95% CI
Severe perio.	1.74	1.01, 3.0
BMI (>27)	4.77	4.1, 5.6
HDL (≤40)	2.2	1.7, 2.9
TRIG (>200)	2.7	2.0, 3.6
CRP	1.3	1.1, 1.5
Diabetes	4.72	2.6, 8.4

Other covariates controlled in model were age, race/ethnicity, exercise, white blood cell count, fibrinogen.

Periodontal Infection
Its Effect on Glycemic Control:

Observational Studies

Epidemiologic Evidence: Incidence of poor glycem. control at ~2-yr follow-up in the Pima Indians

Legend:
- Bone loss < 50%
- Bone loss 50%+

Y-axis: PERCENT with HbA1 9%+

Data (Age Groups):
- 20-34: 13, 50
- 35-44: 20, 38
- 50-64: 18, 5

X-axis: Age Groups

N for bone loss < 50% = 56
N for bone loss 50%+ =49
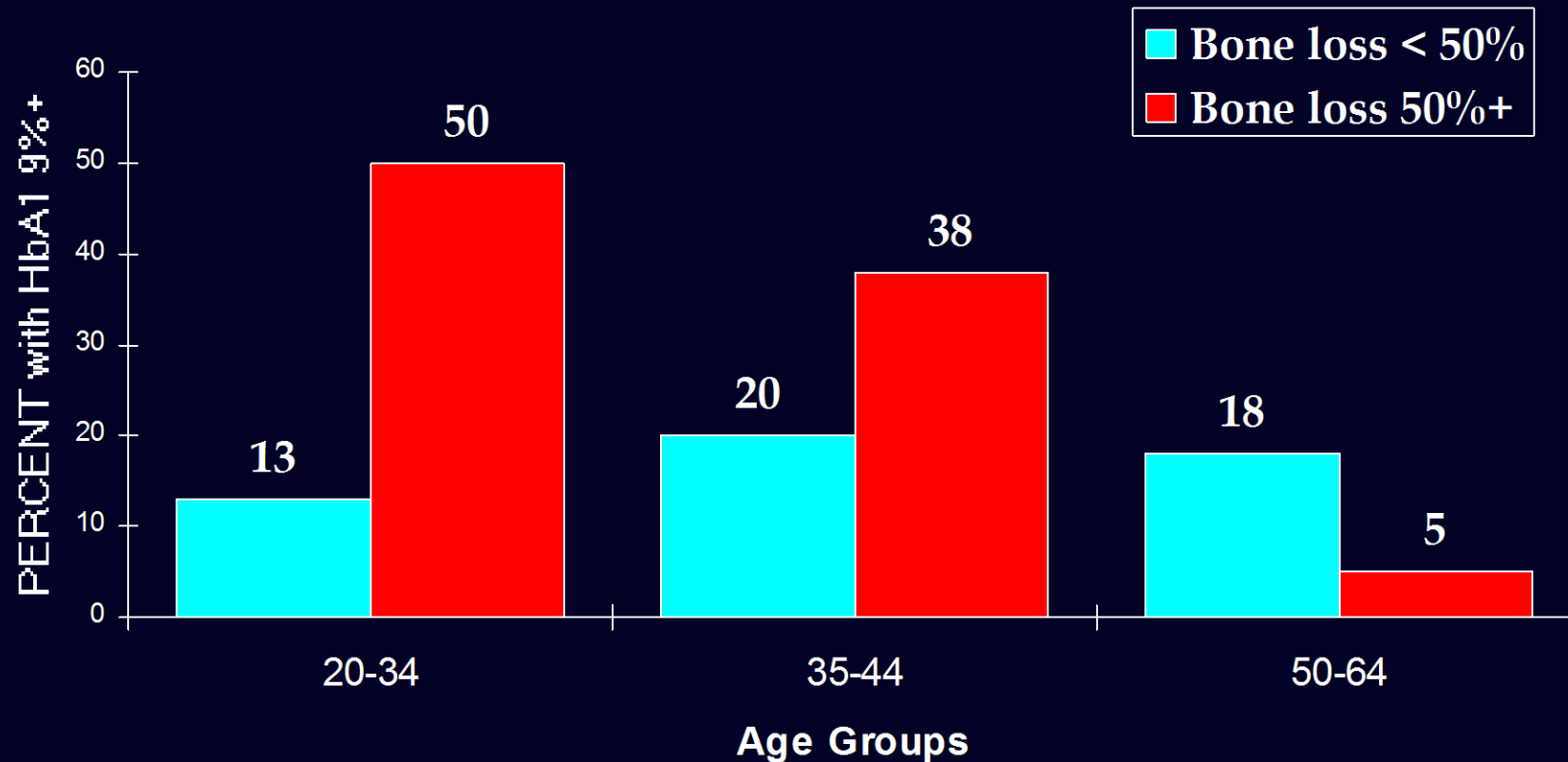
Source: Taylor et al., 1996

Prevalence of poorer glycemic control in U.S. adults, ages 45+, by periodontal status*
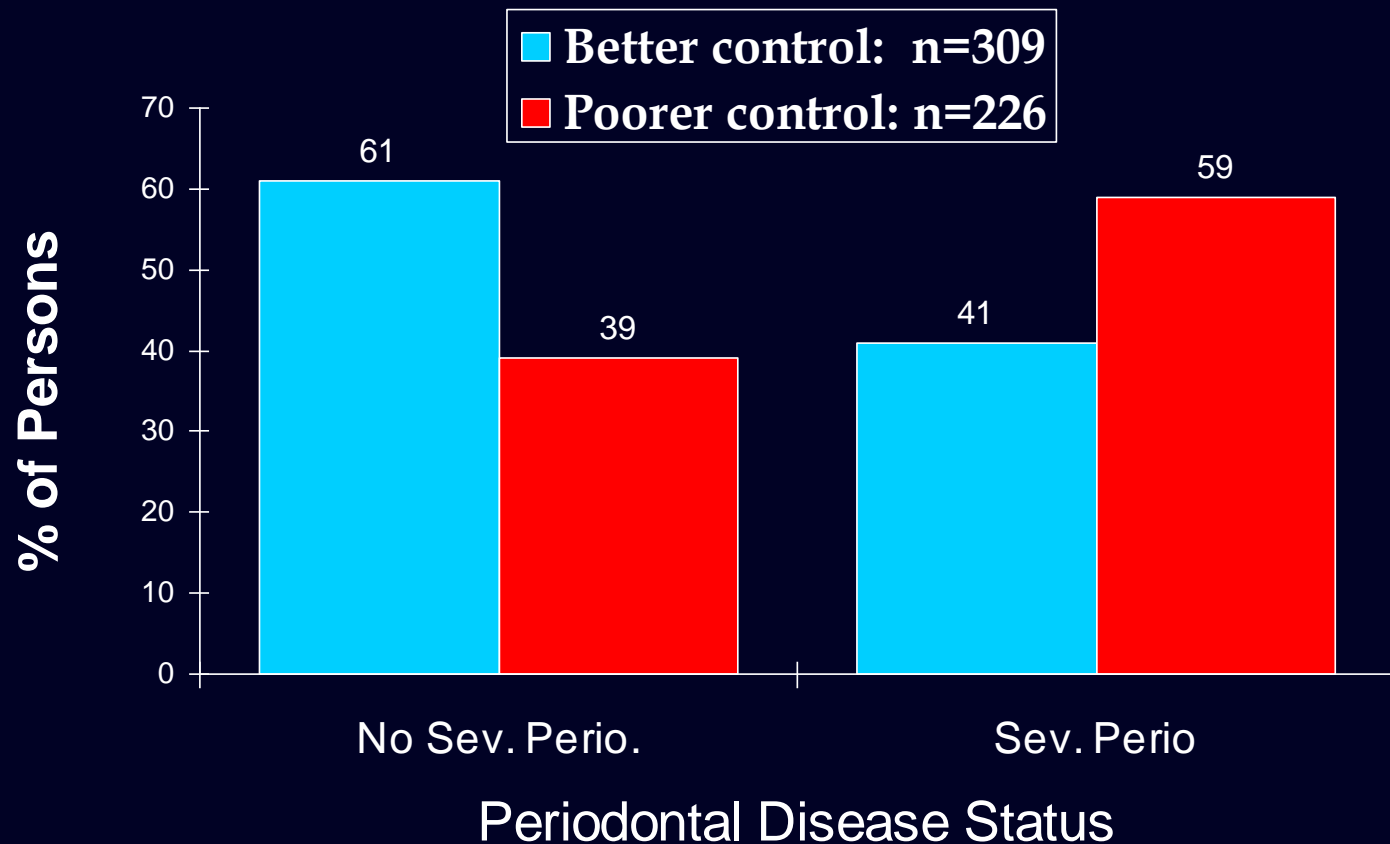
* Sev. Perio=1+ site w LPA 6 mm+, gingival bleeding

Source: NHANES III (1989-94), US Population

Association between severe periodontitis and glycemic control: N=535

Crude Odds Ratio: 3.20 (1.47, 6.98)

	Glycemic Control	
Periodontal Status	Better HbA1c < 8%	Poorer HbA1c ≥ 8%
Sev. Perio: NO	270 (61%)	170 (39%)
Sev. Perio: YES	39 (41%)	56 (59%)

Logistic regression model: poor glycemic control in U.S. adults, ages 45+, non-smoking, NHANES III

COVARIATE	OR	95% CI
Severe perio.	4.9	2.0, 11.9
Taking Diab med	3.4	1.7, 5.8
BMI (≥ 27)	2.6	1.2, 5.4
TRIG (>200)	2.7	2.0, 3.6
CRP (>1.0)	2.6	0.5, 13.8
Exercise	1.0	0.99, 1.01

Other covariates controlled in model were age, race/ethnicity, sex, education, poverty income ratio, and MD and DDS visits.

Periodontal Infection
Its Effect on Glycemic Control:

Non-surgical Periodontal Treatment Studies

Locations of clinical therapeutic studies
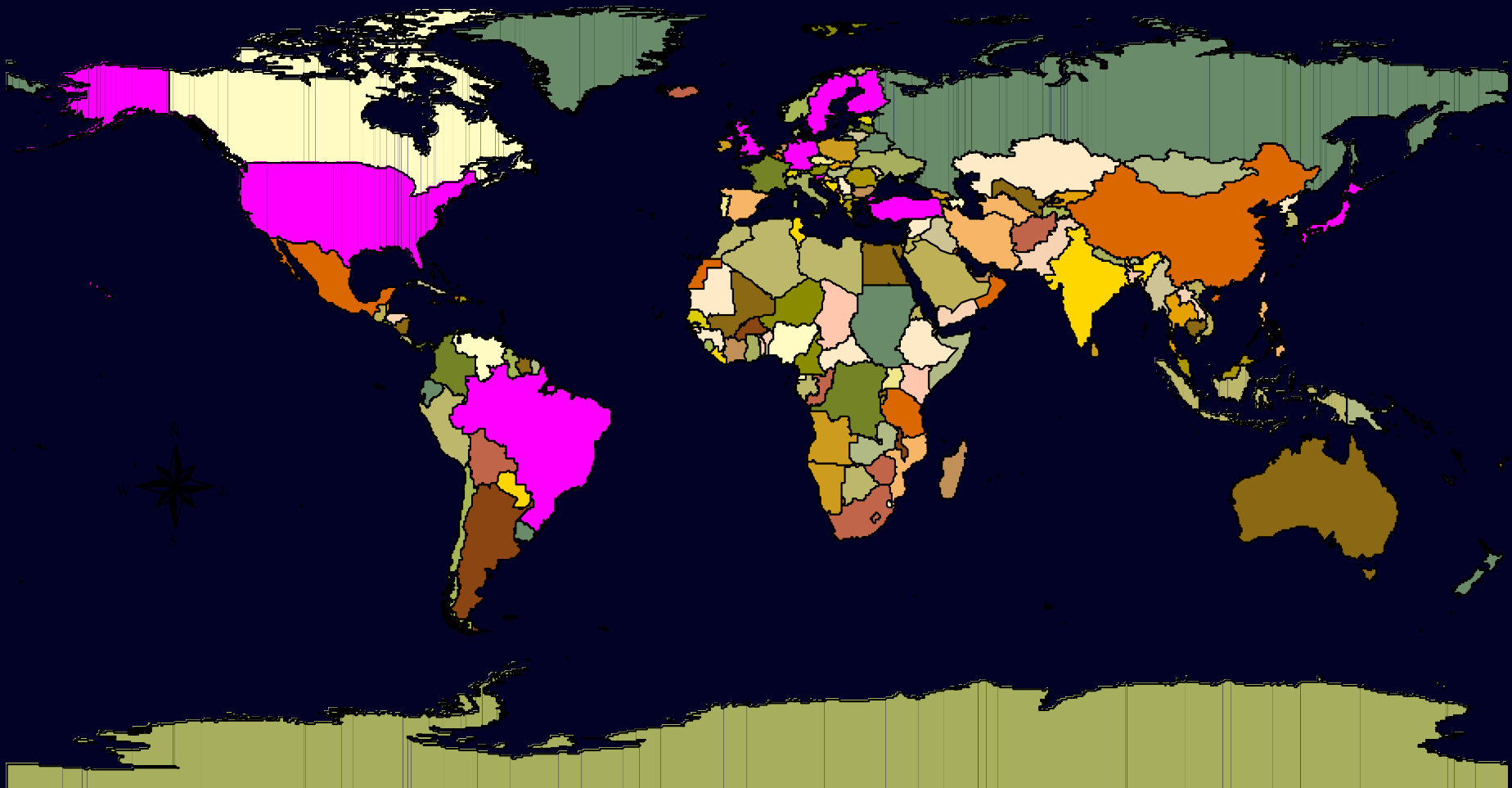
Non-surgical periodontal therapy studies: organizing the evidence AKA "sorting the apples and oranges"

◆ Randomized clinical trials (RCT)
  - ◆ Non-treated control group: 1 positive/3 studies
  - ◆ Positive control group: 3 positive/3 studies

◆ Non-randomized clinical treatment studies (non-RCT)
  - ◆ Non-treated control group: 1 positive/2 studies
  - ◆ No control group: 5 positive/8 studies

Non-surgical periodontal therapy: a meta-analysis. Janket et al. J Dent Res, 2005
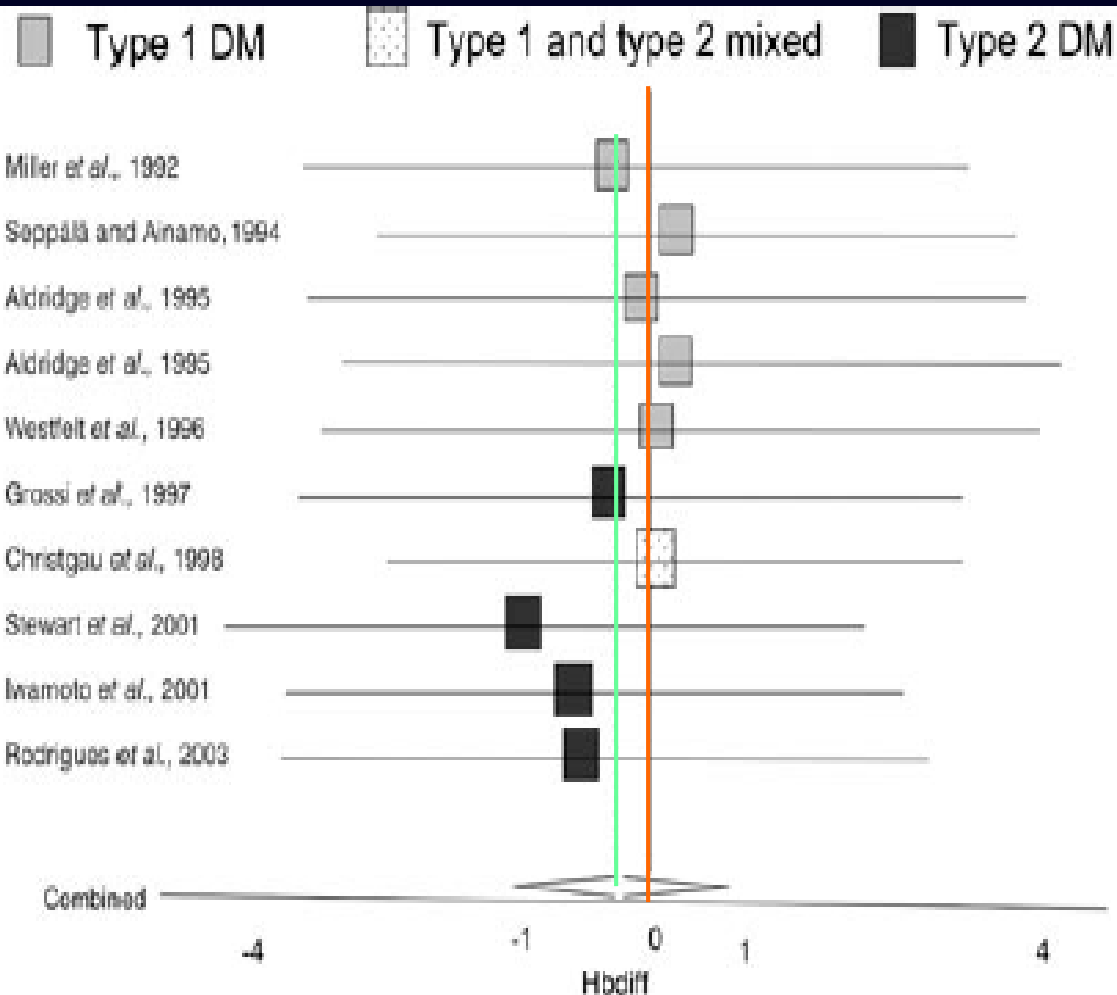
	Weighted Average Change in HbA1c	95% Confidence Interval
All intervention studies	- 0.4%	- 1.5, 0.7
Studies of type 2 DM only	- 0.7%	- 2.2, 0.9
Non-surgical debridement only	- 0.4%	- 2.1, 1.3
Antimicrobial intervention in type 2 diabetic patients	- 0.7%	- 2.3, 0.9

Treating Periodontal Infection: Effects on Glycemic Control

◆ **University of Michigan**

◆ **SUNY at Buffalo**

◆ **University of North Carolina at Chapel Hill**

◆ **NIH/NIDCR**

Study Design

Perio tx + Doxy.

Group 1

SPT SPT SPT SPT

month   0   3   6   9   12   15

Perio tx + Metron.

Group 2

SPT SPT SPT SPT

month   0   3   6   9   12   15

Prophy + Placebo.   **Perio tx.**

Controls

ssrt ssrt ssrt

month   0   3   6   9   12   15
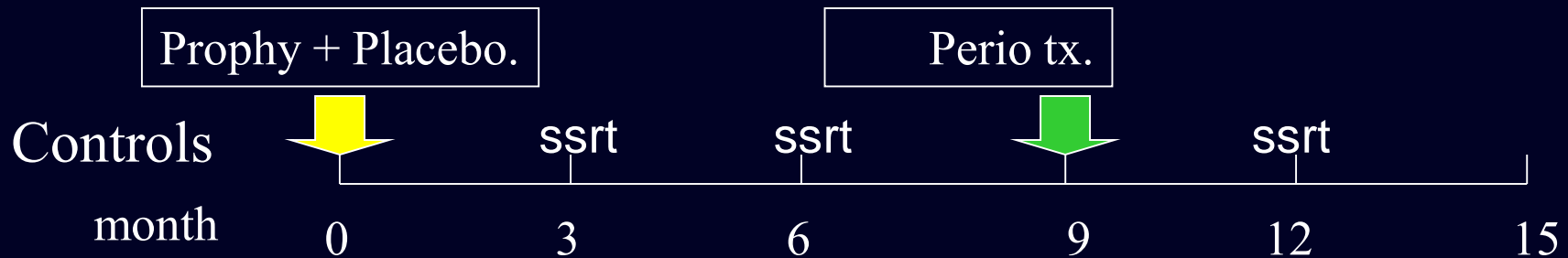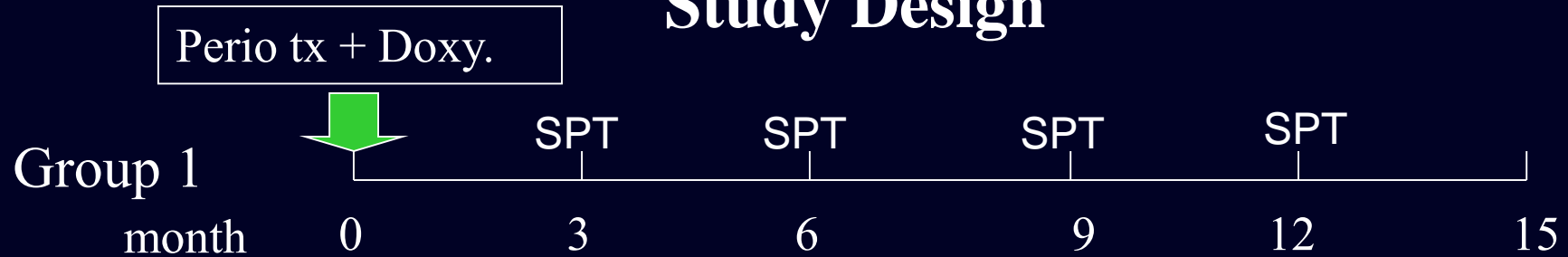
SPT= supportive periodontal therapy, including ssrt
ssrt= site specific rescue therapy

Preliminary results: Improvement in Hemoglobin A1c N=16, 15, 15
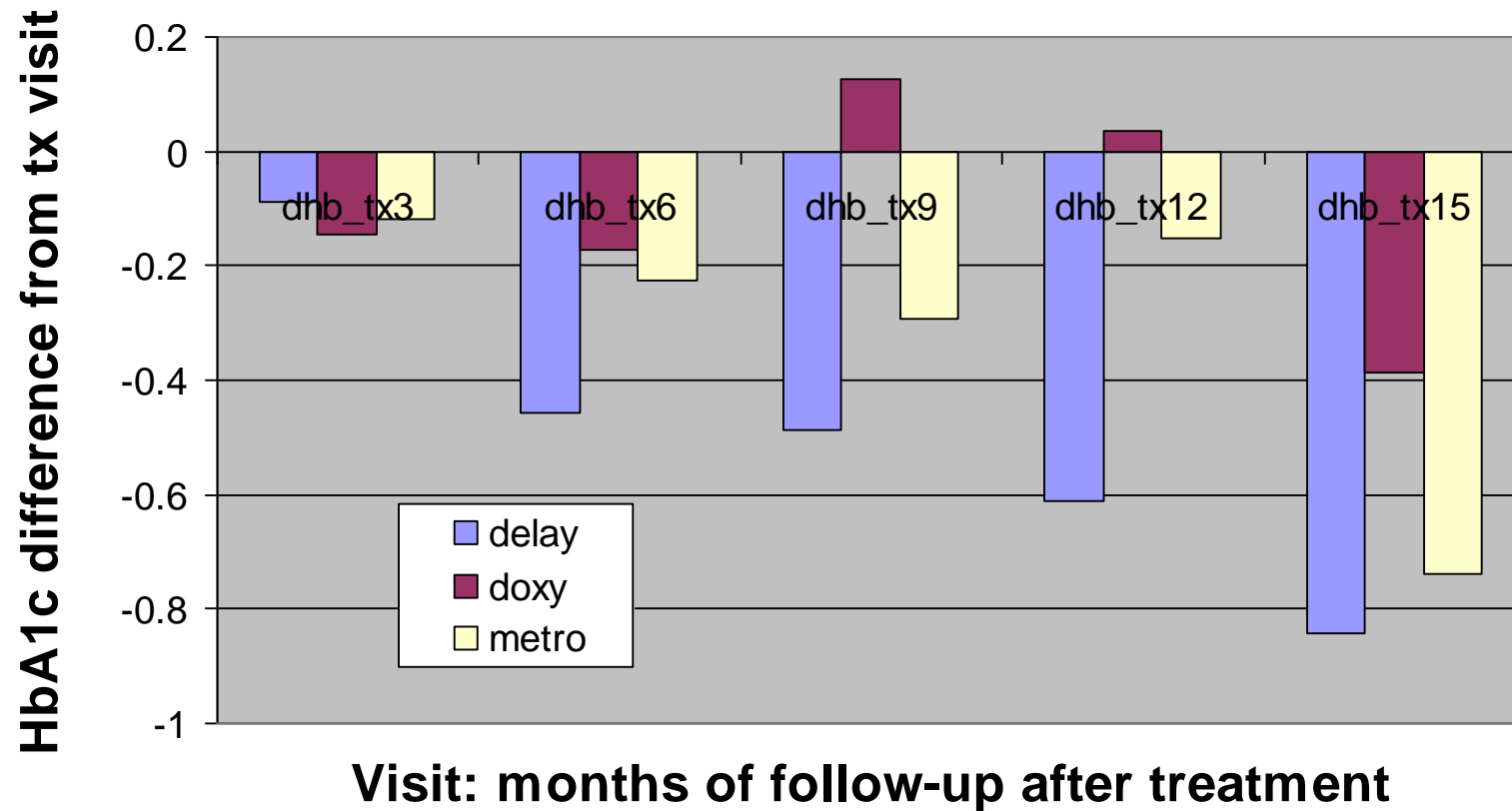
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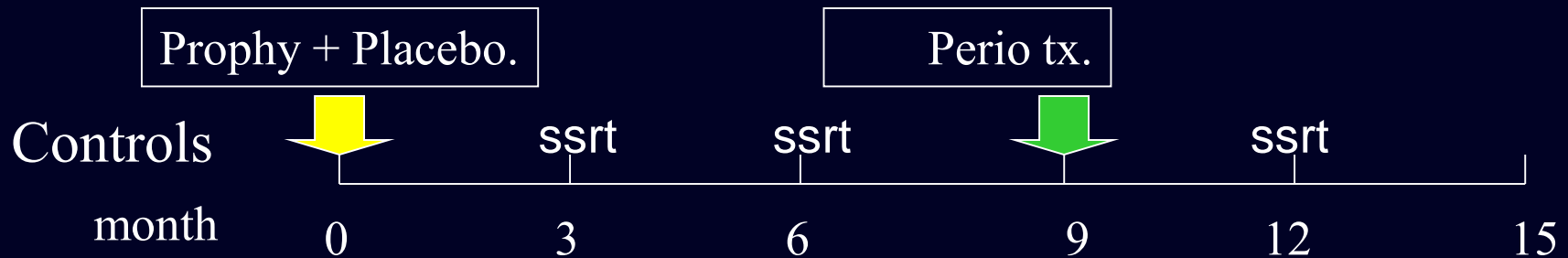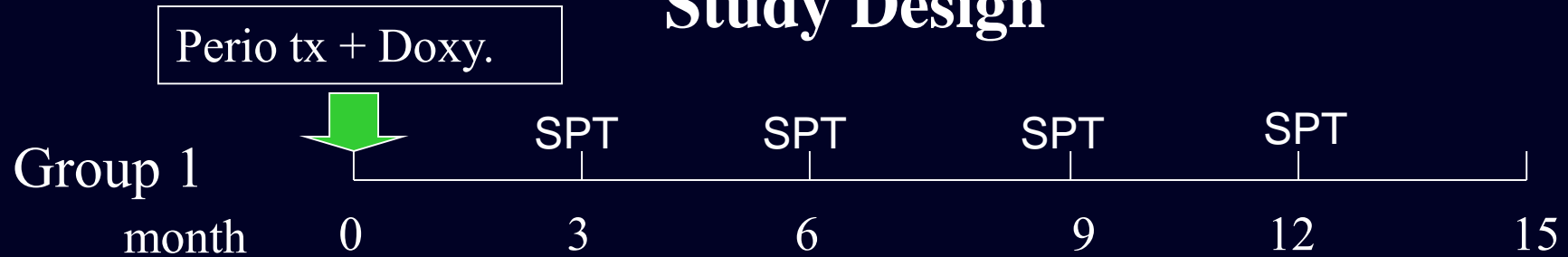
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Overview

- Global overview of diabetes and periodontal diseases prevalence

- Conceptual model of chronic periodontal inflammation and insulin resistance

- Periodontal infection and glycemic control
  - Observational studies
  - Treatment studies

- Significance of improving glycemic control

- Periodontitis and complications of diabetes

- Conclusions

Significance of improving of glycemic control

◆ Any sustained lowering of blood glucose helps delay the onset and progression of microvascular complications of diabetes

◆ Medical complications of diabetes

- ◆ Neuropathy – 50%

- ◆ Any cardiovascular disease – 38%

- ◆ Coronary heart disease – 22%

- ◆ Stroke – 21%

- ◆ Visual Impairment – 23%

- ◆ Kidney disease – 40% of new cases of renal failure due to diabetes

Landmark clinical trials demonstrating the significance of improving of glycemic control

- <u>Diabetes Control and Complications Trial (DCCT)</u>
  - Intensive blood glucose control in type 1 diabetes
  - 35% to 70% reduction in risk of retinopathy, nephropathy and neuropathy
- <u>UK Prospective Diabetes Study (UKPDS)</u>
  - Intensive blood glucose control in type 2 diabetes
  - 12% to 33% reduction in risk of retinopathy and nephropathy

Periodontal infection and complications of diabetes

- Thorstensson et al., 1996; J Clin Periodontol.
  - 39 case-control pairs, type 1 and type 2 diabetes
  - Cases (severe periodontal disease) had greater risk for
    - Proteinuria
    - Cardiovascular complications: stroke, TIA, angina, myocardial infarction, and intermettent claudication

- Saremi et al., 2005; Diabetes Care.
  - Prospective cohort study of n=628, type 2 diabetes
  - Severe periodontal disease: 3.2x greater risk for cardiorenal mortality (ischemic heart disease and nephropathy)
  - Controlled for established risk factors: age, sex, duration, BMI, hypertension, blood glucose, cholesterol, ECG abnormalities, macroalbuminuria, and smoking

Conclusions

◆ Evidence that treating periodontal infection can:

   ◆ Lead to improved glycemic control

   ◆ Possibly prevent, delay, or reduce severity of complications

TREATING PERIODONTAL INFECTION: EFFECTS ON GLYCEMIC CONTROL IN COMMUNITY HEALTH CENTERS

Our Collaboration, funded by NIH/NIDCR

Specific Aims

1. Identify and characterize the population of patients with type 2 diabetes, ages 18+ years, who are listed in the diabetes registry

2. Select a probability sample (n=200) from each center's list to review medical and dental records and the CHC's electronic databases to determine the degree to which information is available and accessible for assessing eligibility

3. Test feasible mechanisms of contacting potential study participants, including telephone, U.S. mail, and face-to-face contact in the medical and dental departments of the CHCs to determine study eligibility and willingness to participate in a clinical examination and interview session, and the yet-to-be planned full-scale RCT

Specific Aims, con't.

4. Determine proportion of the 50 sampled patients from each Center who will present for a clinical examination and interview session

5. Characterize the patients who present for the dental appointment with regards to:
    a. meeting the clinical periodontal disease and medical eligibility criteria,
    b. responses to a set of self-report questions designed to estimate periodontal disease status,
    c. willingness to participate in the full-scale RCT, and
    d. other characteristics influencing periodontal disease status and glycemic control status, including current HbA1c status.

Inclusion criteria

- 18+ years old

- Registered patient at one of the four participating CHCs

- Type 2 diabetes, at least 6 months duration

- At least 6 natural teeth

- Willingness to participate in the pilot clinical examination and interview session

Exclusion criteria

◆ Blood dyscrasias

◆ Pregnancy or breast feeding

◆ Presence of severe cognitive or communicative impairment

◆ HIV+ positive

◆ Cardiac pacemaker

◆ Requiring prophylactic antibiotics before dental treatment

◆ Medically unstable

  ◆ {(e.g. accelerated angina, undergoing medical diagnostic evaluation, and current or recent severe illness or surgery (e.g. end-stage renal disease or terminal cancer)}

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                    │  Informed consent   │
                    └──────────┬──────────┘
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                    │ Screening interview     │
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                    │ script                  │
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                        │ Study visit  │
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│ Brief Phys. Exam:  │──▶│ Interview  │──▶│ Dental exam:         │──▶│ Participant  │
│        Ht.         │   └────────────┘   │ EO &IO soft tissue   │   │ Advise and   │
│        Wt.         │                    │ # teeth              │   │ $25 pymt     │
│        BP          │                    │ Caries status        │   └──────────────┘
│        HbA1c       │                    │ Perio (Pck, BOP)     │
└────────────────────┘                    └──────────────────────┘
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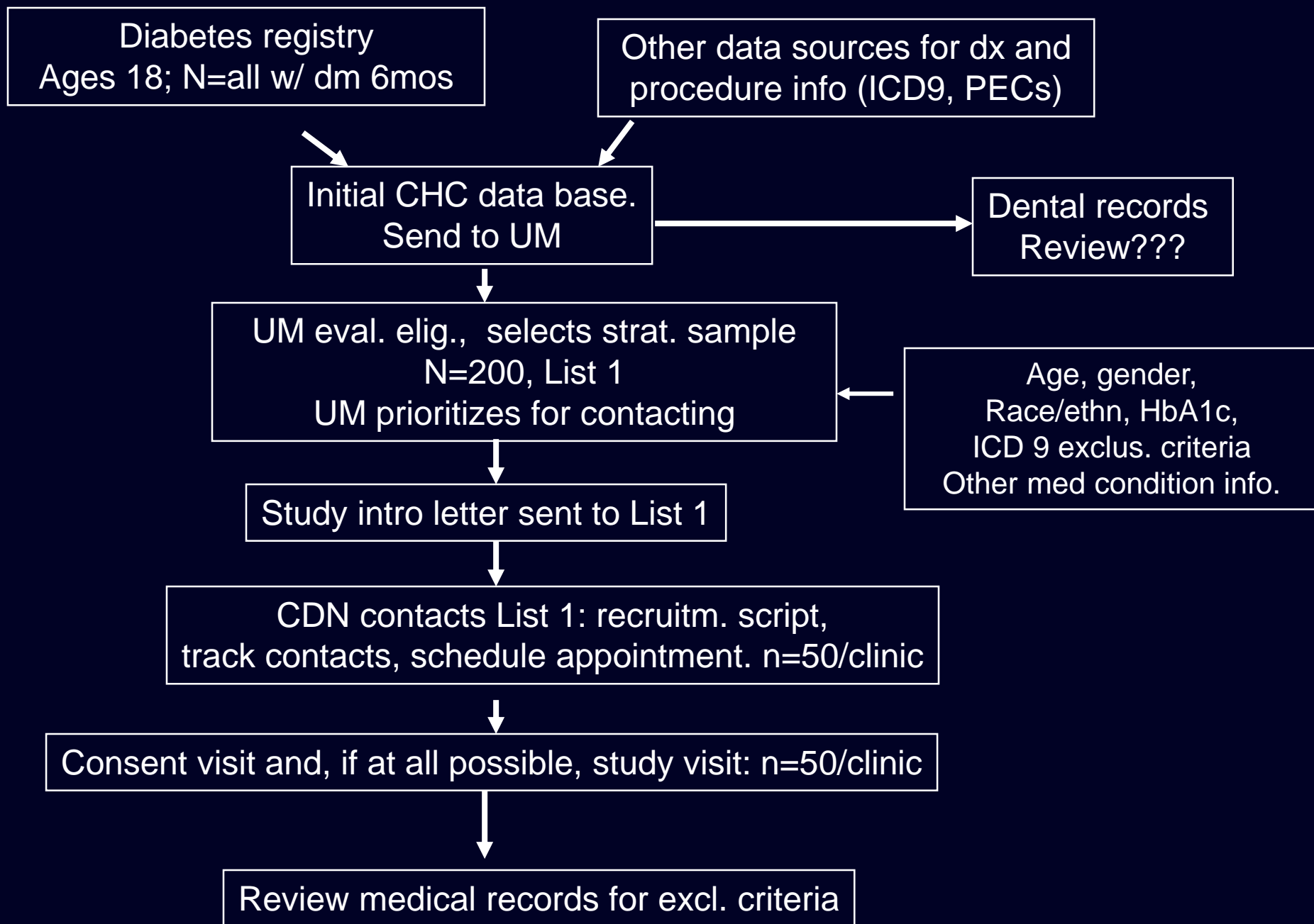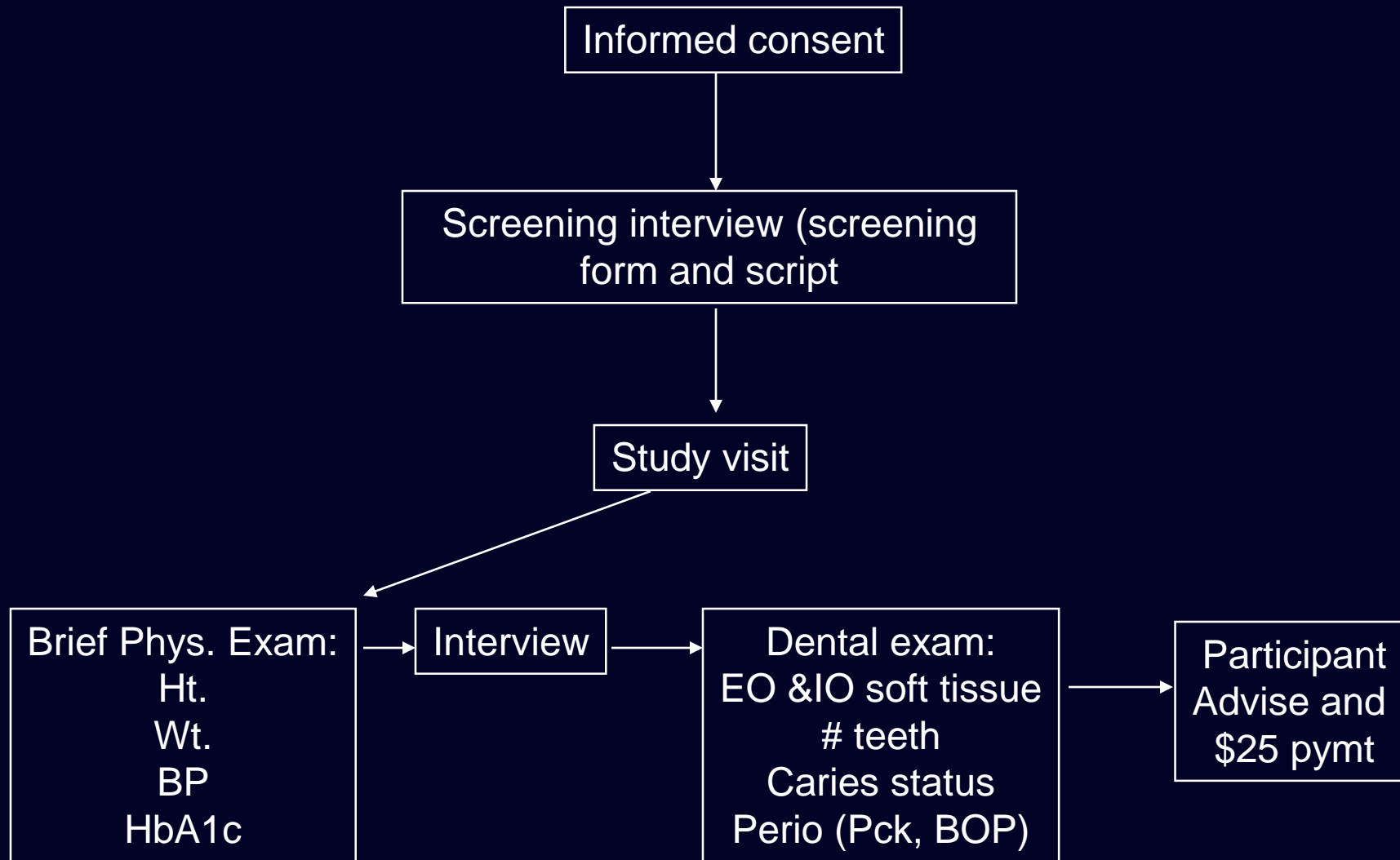
Outcomes anticipated for our project

◆ Evaluation of feasibility of conducting randomized clinical trial (RCT)

◆ Prelim data for *planning grant (R-21)* to plan multi-center RCT (Feb 1 or June 1, 2007 submission)

◆ Prelim data for *multi-center RCT proposal (U-01)*

Thank you for your attention

◆ Please feel to contact me:

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