Diabetes Mellitus and Periodontal Diseases

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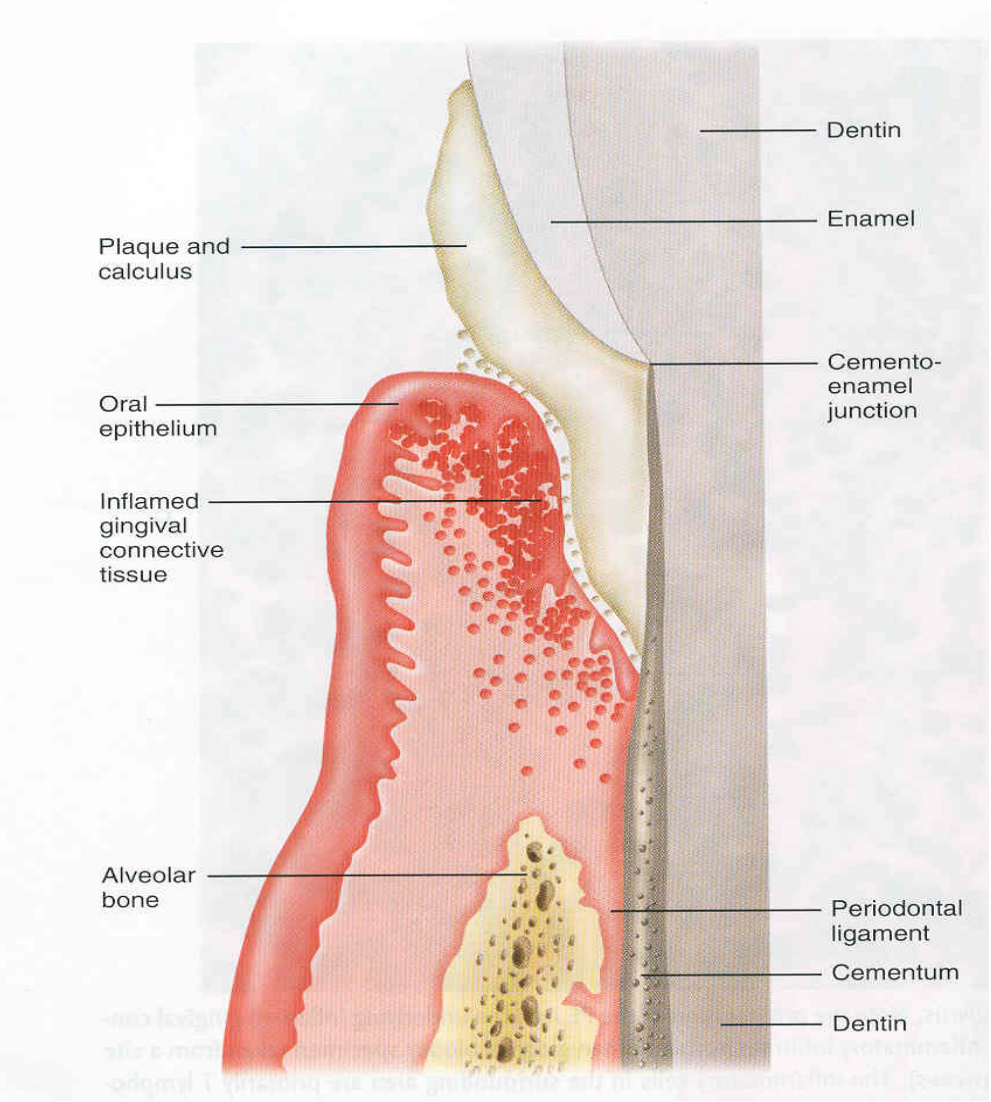
Department of Periodontology

Objectives
Diabetes Mellitus

- Review of periodontitis and prevalence
- Diabetes and prevalence
- What is the connection?
- Research design exercise
- How does this relate to patient care?

Periodontitis

- **Inflammation combined with attachment loss**
- The connective tissue attachment is destroyed, bone loss, and the junctional epithelium migrates apically down the root
- If the gingival margin does not recede this results in a periodontal pocket



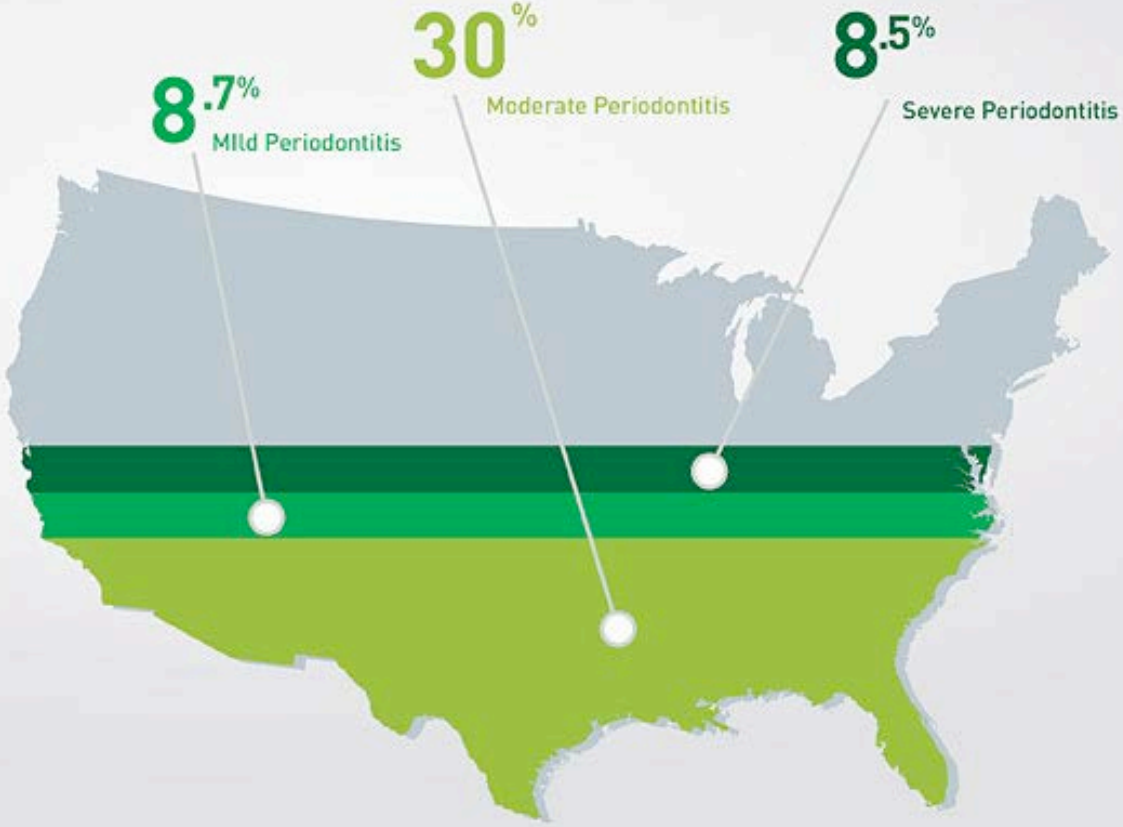
*THE AMERICAN ACADEMY OF PERIODONTOLOGY WARNS OF A SIGNIFICANT PUBLIC HEALTH PROBLEM

HALF OF AMERICAN ADULTS SUFFER FROM GUM DISEASE

47.2%
Have periodontitis

THAT'S

64.7
Million
Adults 30 years and older



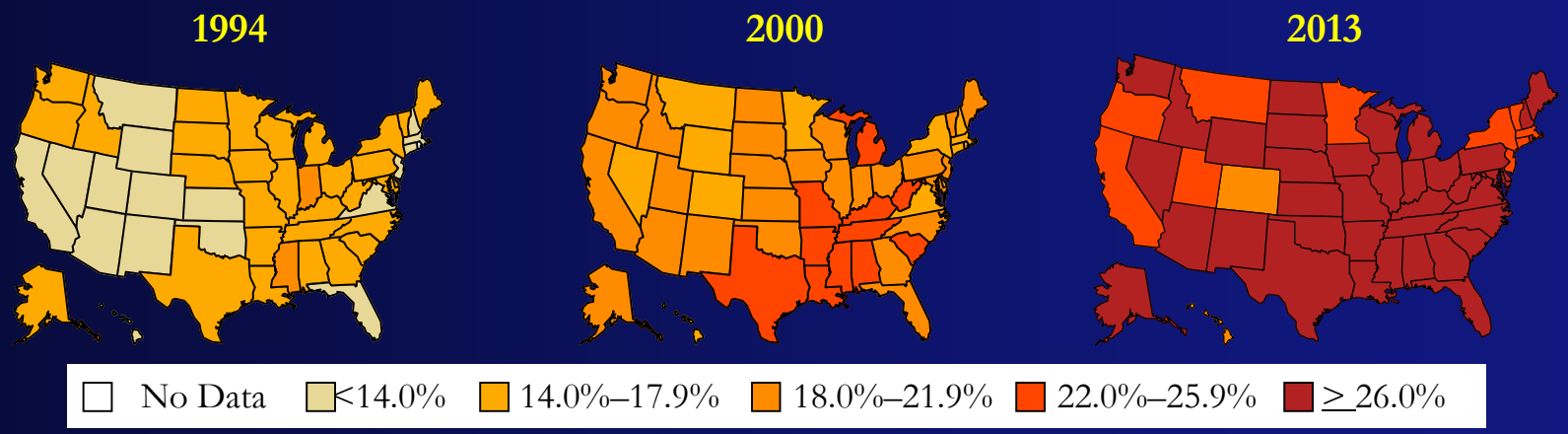
*SOURCE: P.I. Eke, B.A. Dye, L. Wei, G.O. Thornton-Evans, and R.J. Genco. Prevalence of Periodontitis in Adults in the United States: 2009 and 2010. J DENT RES 0022034512457373, first published on August 30, 2012 as doi:10.1177/0022034512457373

Diabetes Mellitus

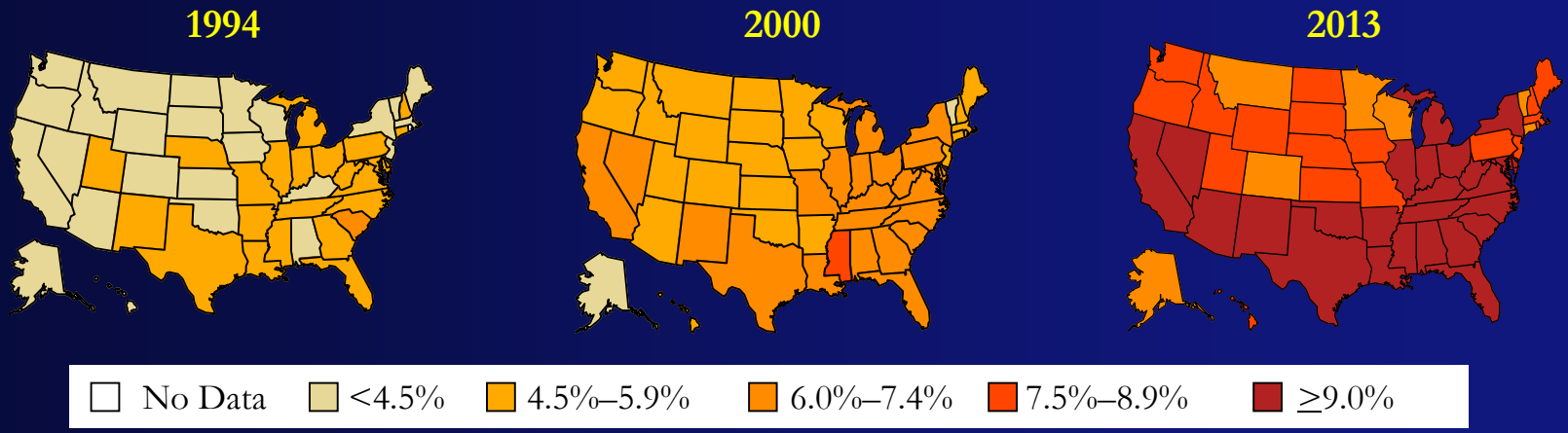
Definition: Altered glucose tolerance or impaired lipid and carbohydrate metabolism

Age-adjusted Prevalence of Obesity and Diagnosed Diabetes Among US Adults

Obesity (BMI ≥30 kg/m^2)

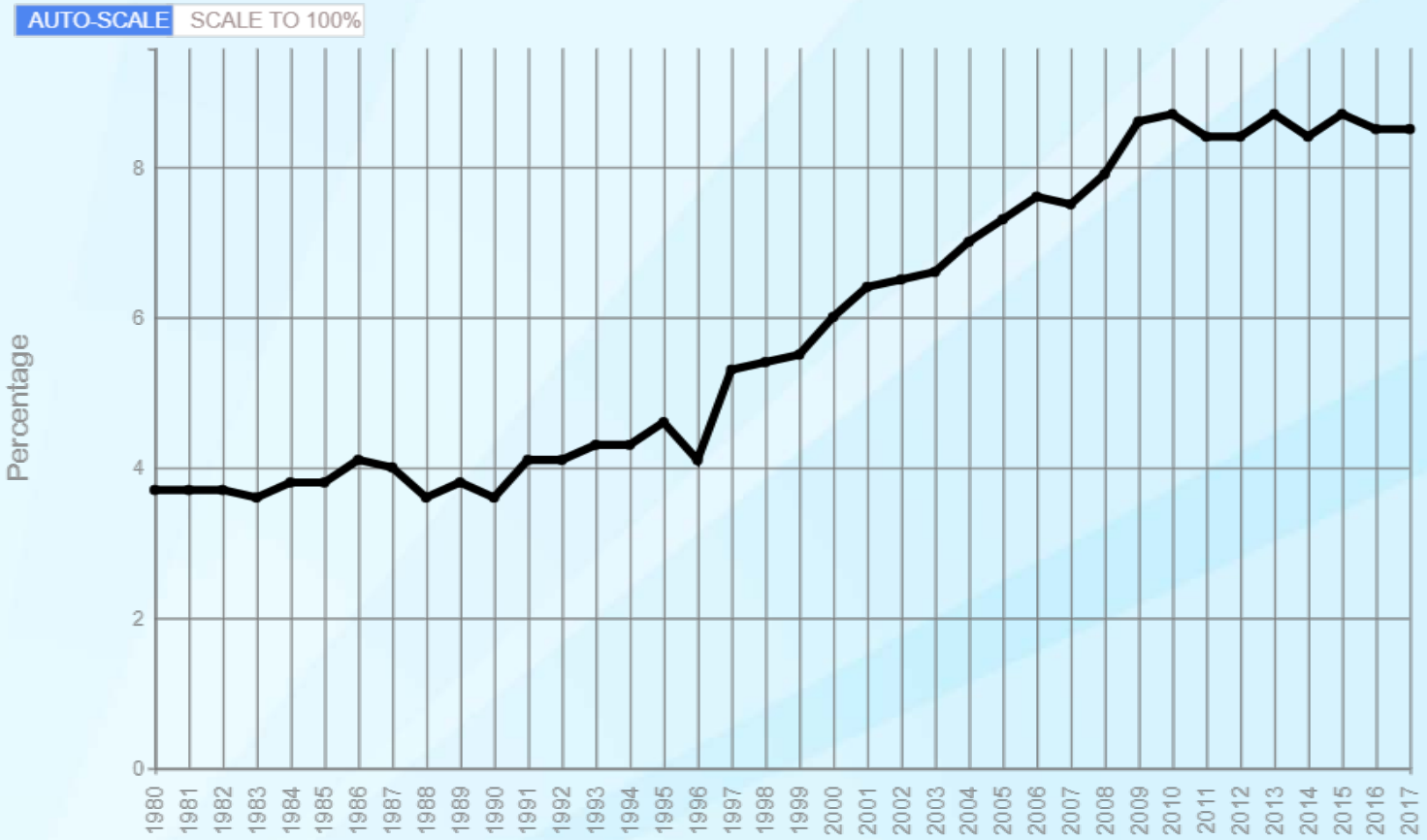


Diabetes



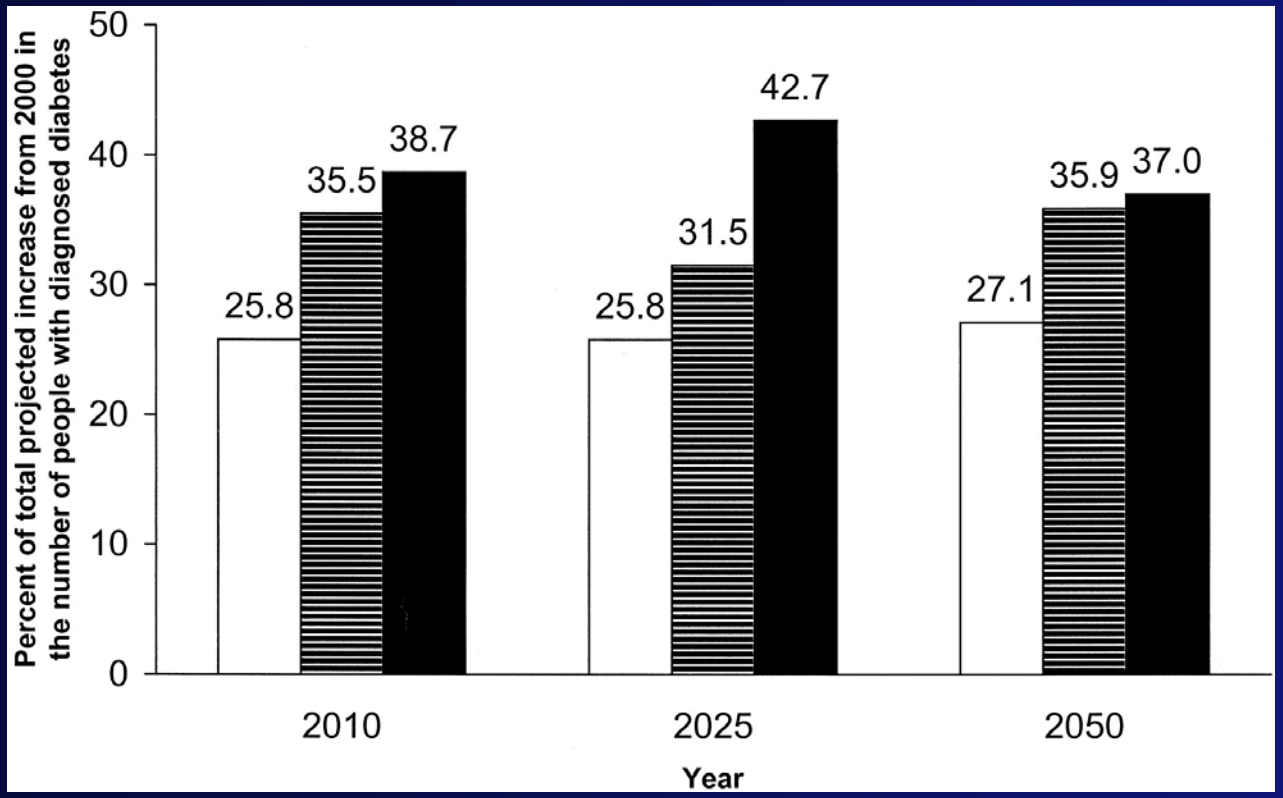
CDC's Division of Diabetes Translation. National Diabetes Surveillance System available at http://www.cdc.gov/diabetes/statistics

Diagnosed Diabetes, Total, Adults Aged 18+ Years, Age-Adjusted Percentage, National



Division of Diabetes Translation

Percentage breakdowns of the projected increase in the total number of people with diagnosed diabetes



Population growth

increasing prevalence rates

demographic changes

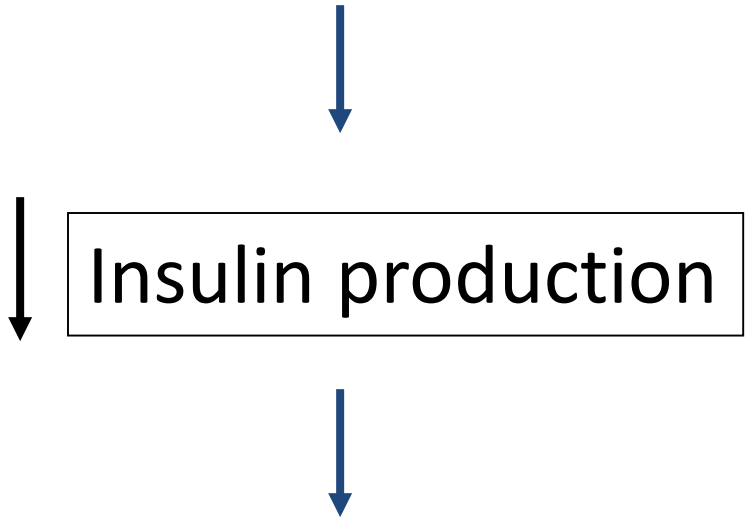
James P. Boyle et al. Diabetes Care 2001;24:1936-1940

American Diabetes Association.

Diabetes Mellitus Complications

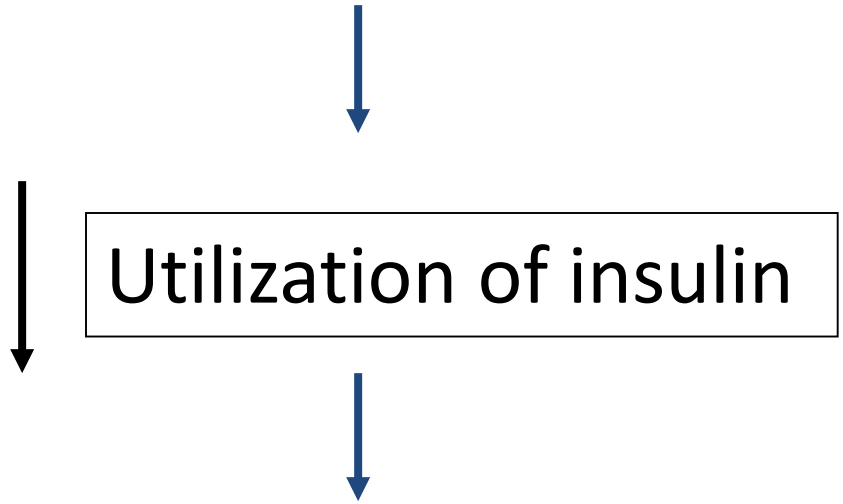
- Diabetic retinopathy → blindness
- Diabetic nephropathy → end-stage renal disease
- Accelerated cardiovascular disease → death
- Lower extremity amputation
- Periodontitis

Autoimmune destruction of the insulin producing beta cells of the pancreas



Type 1 Diabetes Mellitus (T1DM)

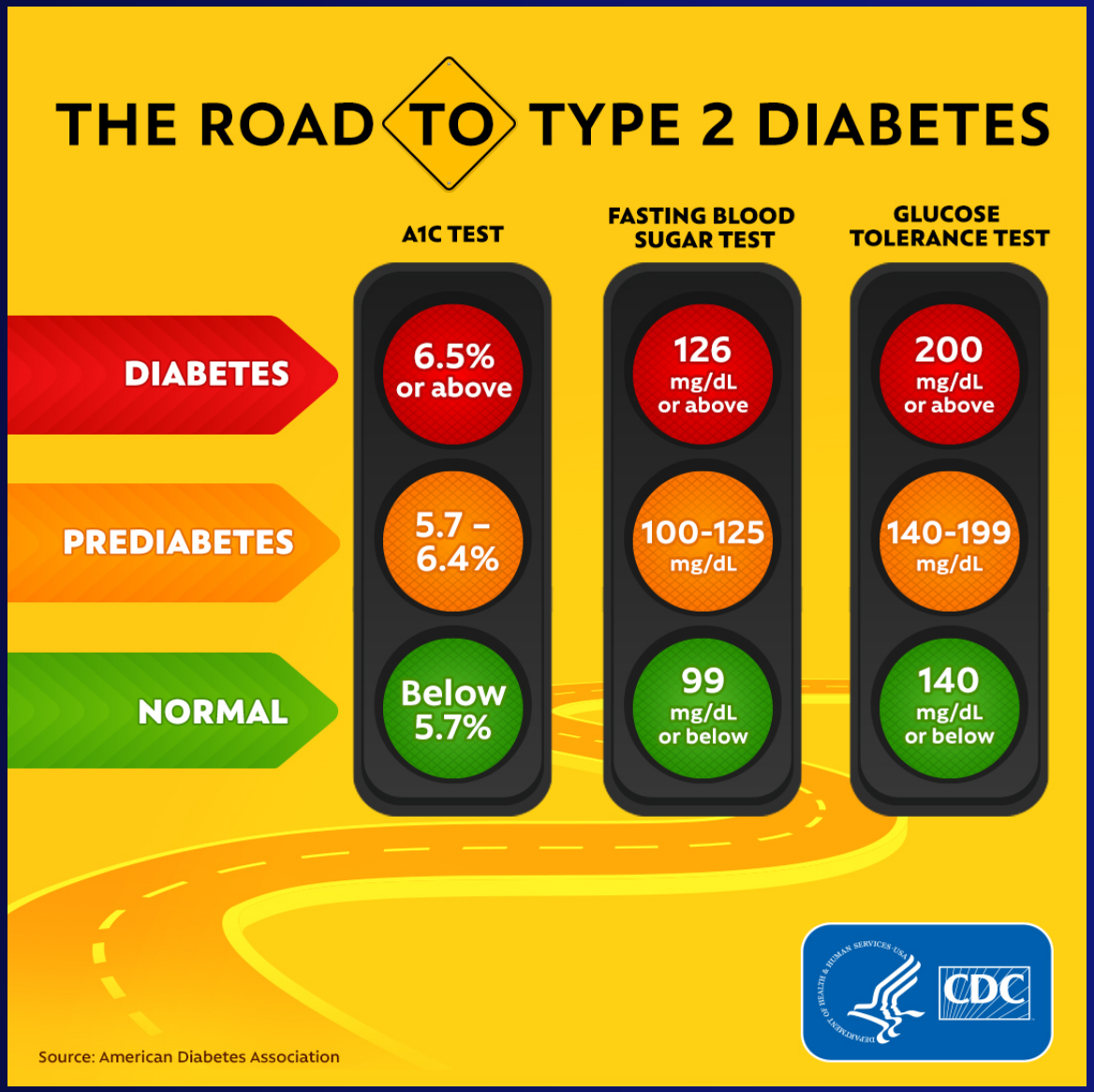
Defects in the insulin molecule or altered cell receptors for insulin



Type 2 Diabetes Mellitus (T2DM)

Blood glucose tests

- Fasting (FPG) and non-fasting plasma glucose (casual)
- Oral glucose tolerance tests (OGTT)
- Glycated hemoglobin test (HbA1 or HbA1c) – measures glucose irreversibly bound to the hemoglobin molecule (30-90 day history)


THE ROAD TO TYPE 2 DIABETES
A1C TEST
FASTING BLOOD SUGAR TEST
GLUCOSE TOLERANCE TEST
DIABETES
PREDIABETES
NORMAL
6.5% or above
5.7 – 6.4%
Below 5.7%
126 mg/dL or above
100-125 mg/dL
99 mg/dL or below
200 mg/dL or above
140-199 mg/dL
140 mg/dL or below
Source: American Diabetes Association

Medical Treatment

↓Lower blood glucose levels

↓Complications of disease

T1DM – insulin replacement therapy

T2DM – diet control, weight control, and oral medications

Diabetes Control and Complications Trial (DCCT)

- Multi-center study of 1,441 T1DM patients
- Two groups: conventional insulin regimens or "tight control" regimen
- 6.5 years

50-75% ↓

Complications:
- Eye
- Kidney

United Kingdom Prospective Diabetes Study (UKPDS)

- 5,000 T2DM patients
- Aggressive reduction of blood glucose using oral medications and insulin

25% ↓

Complications:
- Retinopathy
- Nephropathy

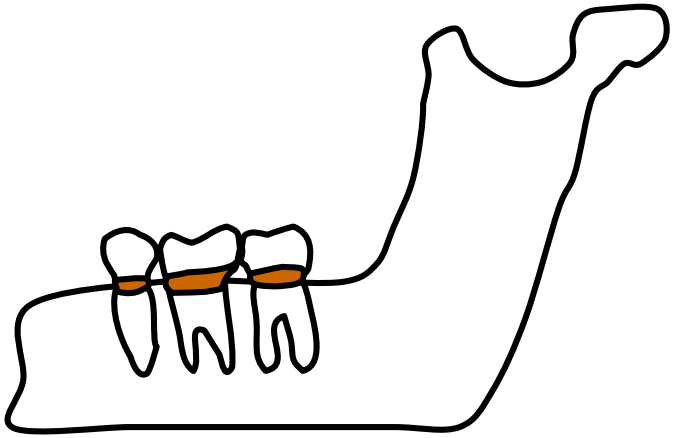
What is the connection between diabetes and periodontal disease?

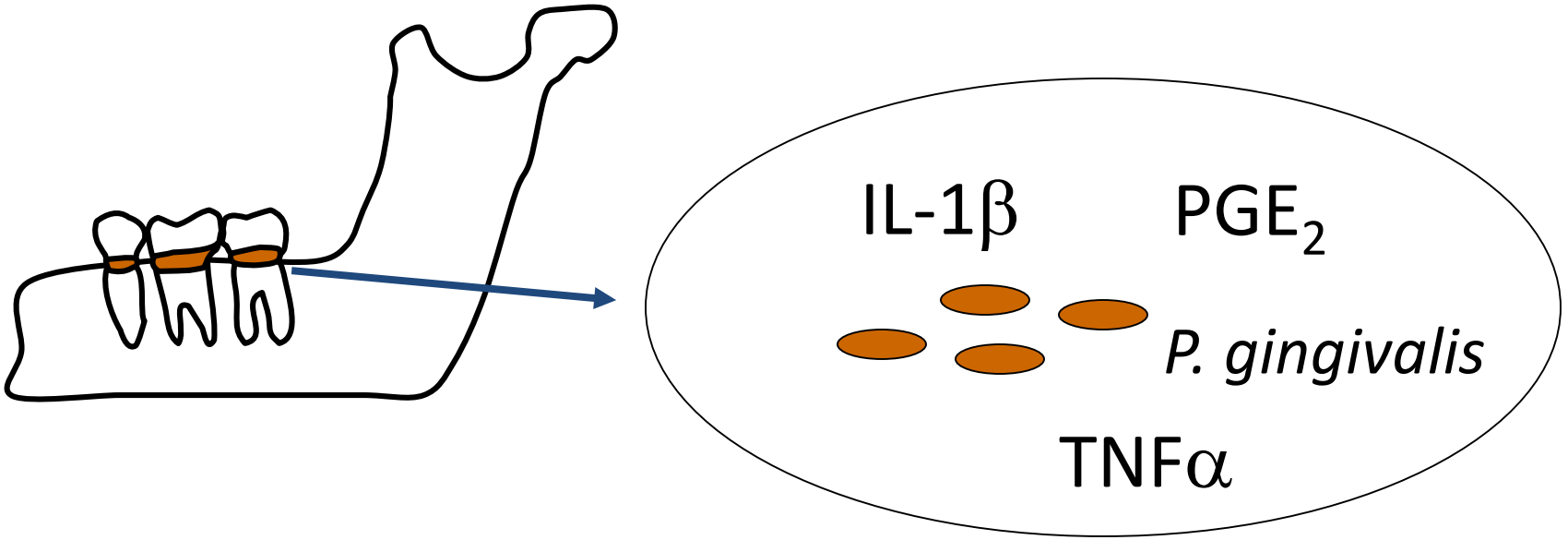
Periodontal Diseases and Diabetes

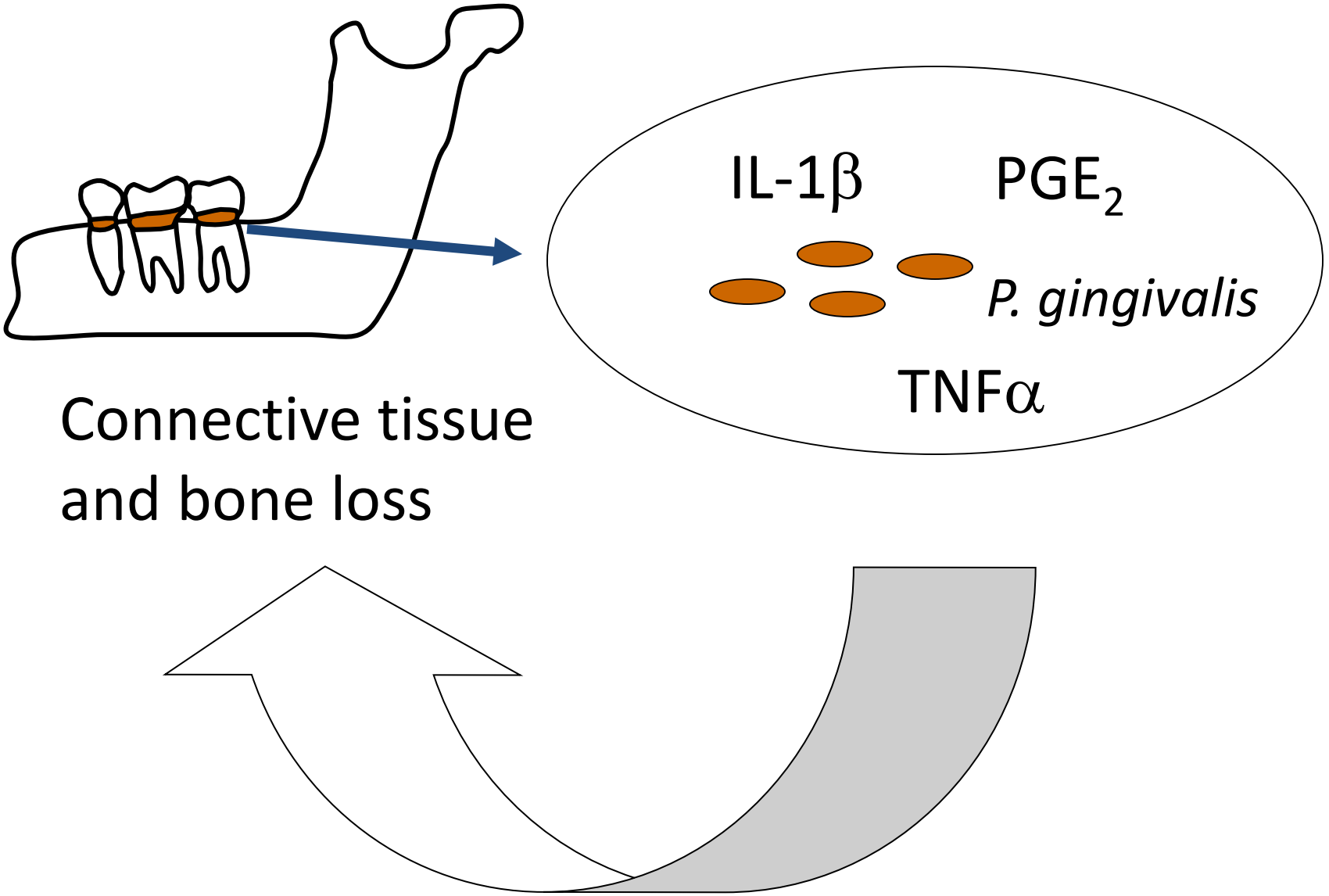
- Periodontitis as an infection may adversely influence glycemic control (analogous to other infections)
- Periodontitis may increase systemic inflammation (systemic inflammation is linked to insulin resistance)
- Periodontal disease may be associated with other diabetic complications

How might diabetes affect the periodontium?

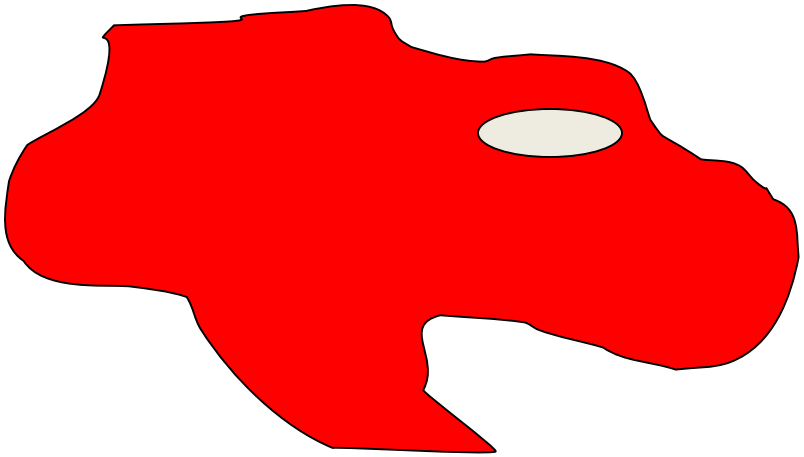
- Microvascular damage
- Impaired collagen metabolism – breakdown/repair
- Advanced glycation end product formation – pro-imflammatory
- Altered subgingival microbiotia
- Impaired host defense
- Increased gingival crevicular fluid glucose concentration




IL-1β
PGE2
P. gingivalis
TNFα


IL-1β
PGE2
P. gingivalis
TNFα
Connective tissue
and bone loss

‘The Angry Macrophage’



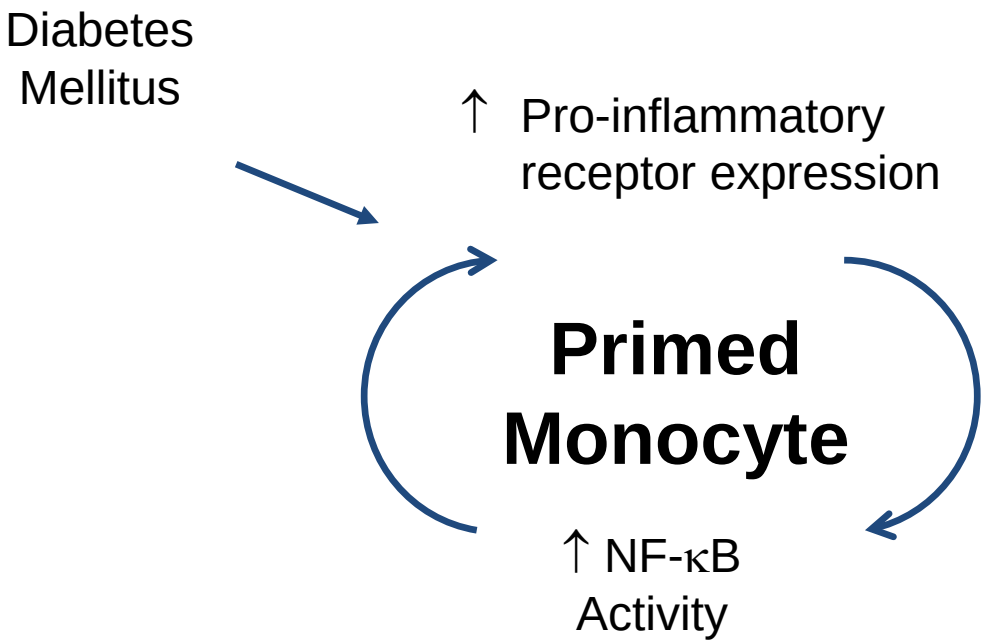
‘Hypersecretory monocyte trait’

Salvi et al. (1998)

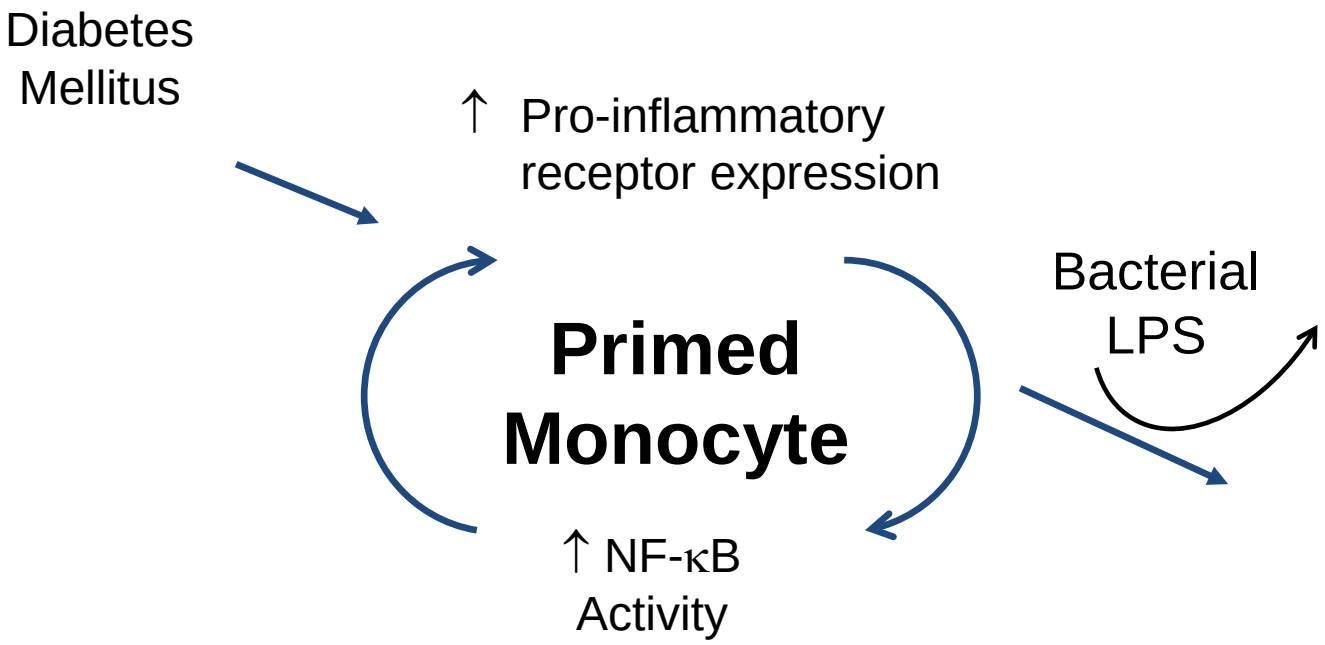
Proposed model

Diabetes
Mellitus

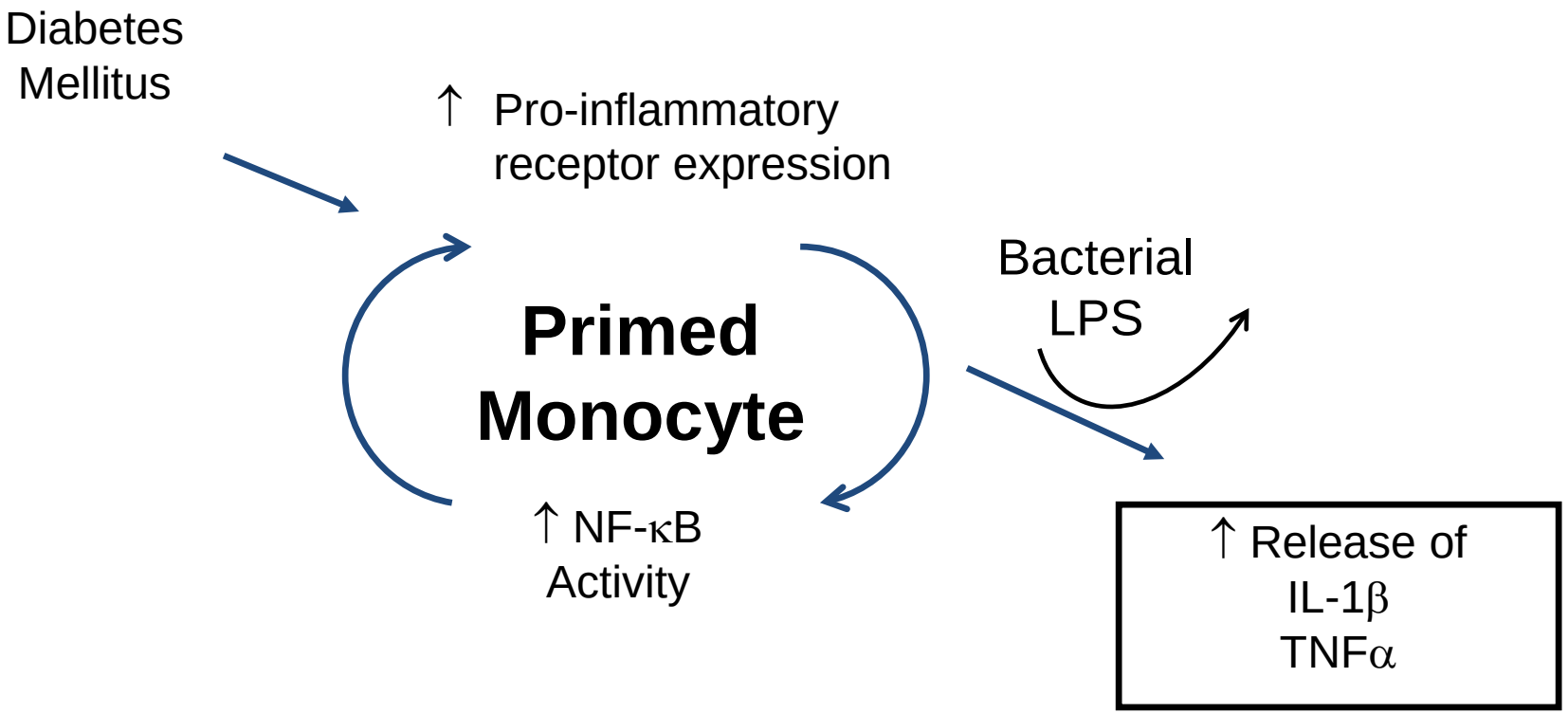
Proposed model



Proposed model



Proposed model



Research Study Design Exercise

Design a study to investigate the connection between diabetes and periodontitis

- Epidemiology – population study of possible connection
- Interventional trial
- Connection with overall/systemic health

Periodontitis and Diabetes

- Prevalence of periodontitis greater in diabetic population (T1 and T2) than non-diabetic populations (Emrich, 1991; Schlossman, 1990)
- Degree of glycemic control may affect risk of severe periodontitis – poor glycemic control 3 times more likely to have severe periodontitis (Tsai, 2002)
- Risk of progressive bone loss over time is greater when glycemic control of diabetes is poor (Taylor, 1998)

Type 2 diabetes mellitus and periodontal diseases

Pima Indian studies, high prevalence of T2DM (Genco et al.)

- 3,219 subjects, glucose tolerance test, measured attachment and bone loss
- Subjects with T2DM were approximately 3 times more likely to have periodontal disease compared to non-diabetic individuals
- *DM patients with poor glycemic control had a much greater risk of progressive bone loss than well-controlled subjects*

Periodontitis and mortality in Type 2 Diabetes (Diabetes Care, 2005)

- Prospective longitudinal study of 628 subjects 35 years of age
- Pima Indians with type 2 diabetes
- 3 groups classified by radiographs and examination:
  1. no or mild disease
  2. moderate disease
  3. severe periodontitis

Periodontitis and mortality in Type 2 Diabetes

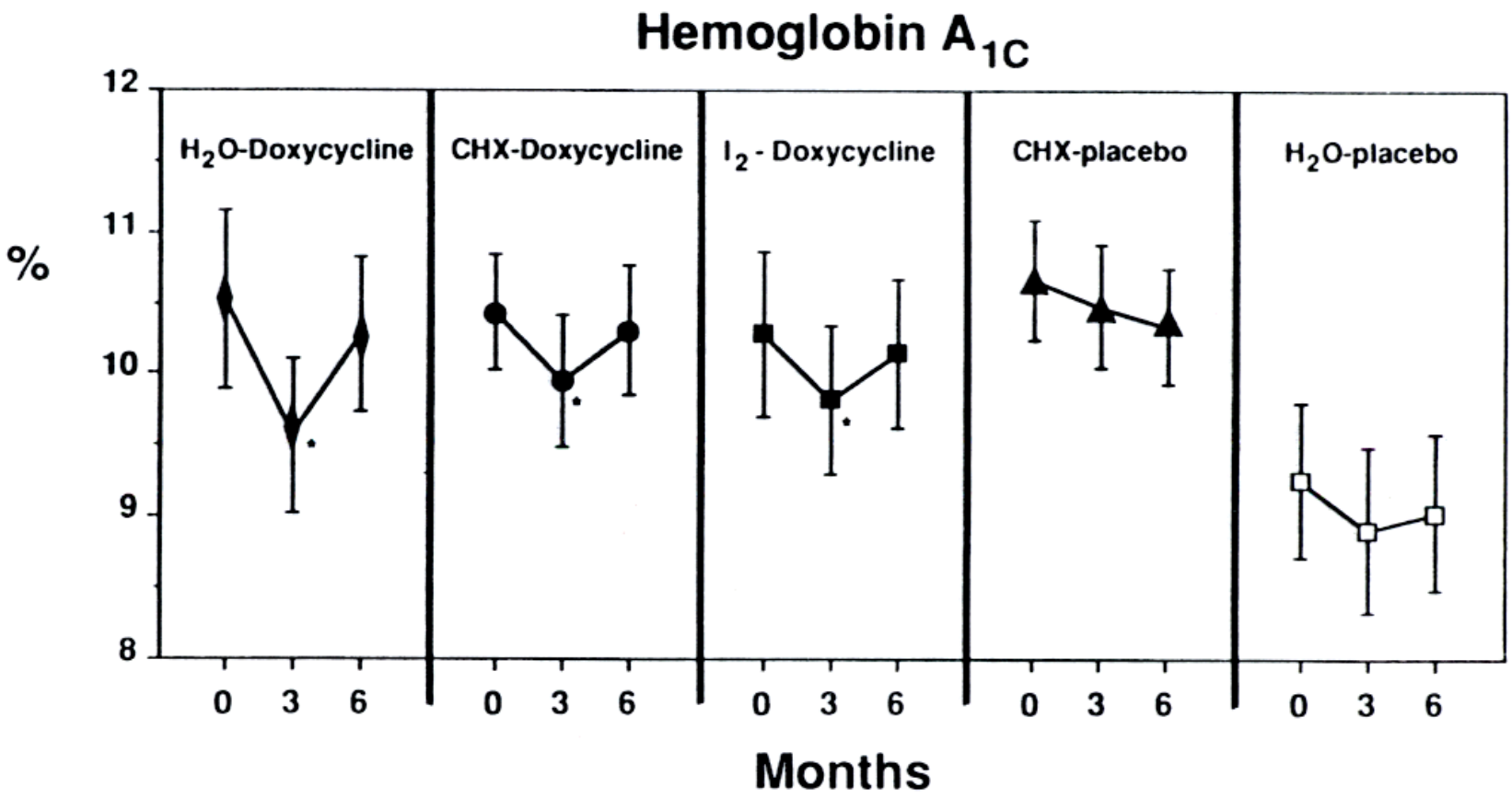
- Median follow-up of 11 years
- 204 subjects had died
- After adjusting for age, gender, duration of diabetes, HbA1c, macroalbuminuria, BMI, cholesterol, HTN, EKG changes, smoking: **subjects with severe periodontitis had 3.2 times the risk of cardio-renal mortality**

Intervential Trial
Periodontal Therapy

Grossi et al. (1997)

Control of periodontal infection by mechanical therapy and systemic antibiotics may improve glycemic control – this effect may be most pronounced in poorly controlled diabetic patients with severe periodontitis

Mean level of glycated hemoglobin at 3 and 6 months after therapy



Diabetes and Dental Outcomes

- Periodontal treatment could improve glycaemic control in diabetic patients. (*Evid Based Dent* 2009; *BMC Oral Health* 2014; *Aust Dent J* 2013)
- The relationship between diabetes mellitus and destructive periodontal disease: a meta-analysis. *Oral Health Prev Dent* 2009
- Dose-response relationship between periodontal inflamed surface area and HbA1c in type 2 diabetics. *J Clin Periodontol* 2009

Diabetes and Dental Outcomes

- Regular dental care may reduce diabetes-specific health care utilization (*Journal of the American Dental Association*, 2012)
- Non-surgical periodontal treatment decreases circulating inflammatory mediators and may be associated with a decrease in insulin resistance in an obese population (*J Periodontology*, 2013)
- Adults with diabetes are at higher risk of experiencing tooth loss and edentulism (*JADA*, 2013)

The Diabetes and Periodontal Therapy Trial (DPTT)

DPTT

- A multicenter randomized single-masked clinical trial supported by the National Institutes of Health (NIDCR)
  - SUNY Stony Brook, NY
  - University of Minnesota
  - University of Alabama at Birmingham
  - University of Texas at San Antonio
  - University of Texas at Houston

Purpose

- Participants with type 2 diabetes
  - 7% < HbA1c <9%
- Moderate to severe chronic periodontitis
- Test the effect of non-surgical periodontal therapy (i.e. scaling and root planing)
- Main outcome: change in blood glucose levels as measured by glycosylated hemoglobin (HbA1c) at 3 and 6 months

Measurement of Blood Sugar Glycated hemoglobin assay (HbA1c)

- Assesses glycemic control over preceding 2-3 months
- Based on glucose binding to hemoglobin in red blood cells

Study Design

- The study compared the 6 month change in HbA1c
  - 300 subjects randomly assigned to receive scaling and root planing (Treatment Group)
  - 300 subjects assigned to delayed treatment (Control Group)
- Subjects were recruited from diabetes care clinics, dental clinics and community practices at the five Clinical Sites.
- 35 years or older, diagnosis of T2DM for at least 3 months with at least 16 teeth
- The proposed sample size was powered to detect a clinically relevant difference of *0.6% in HbA1c reduction within 6 months*

Study Design

Prior to Enrollment/Screening
- HbA1c level
- presence and severity of periodontitis

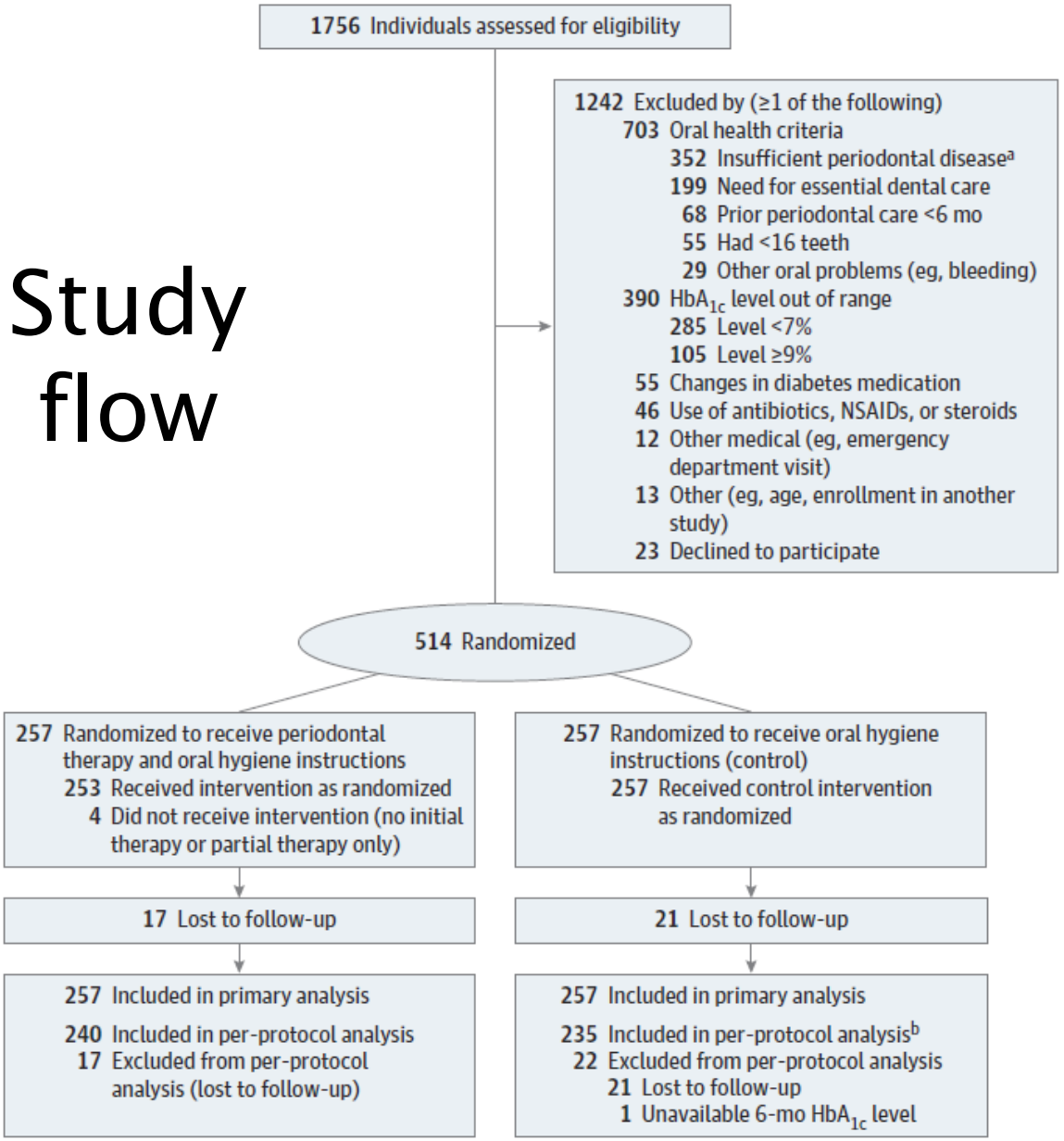
Randomize into one of two groups
- Non-surgical therapy immediately
- Delayed treatment

Dental exam and HbA1c
- 3 months
- 6 months

Results

- 514 participants with T2DM were enrolled and randomized to:
  - Treatment group (n=257)
  - Control group (n=257)

Study flow

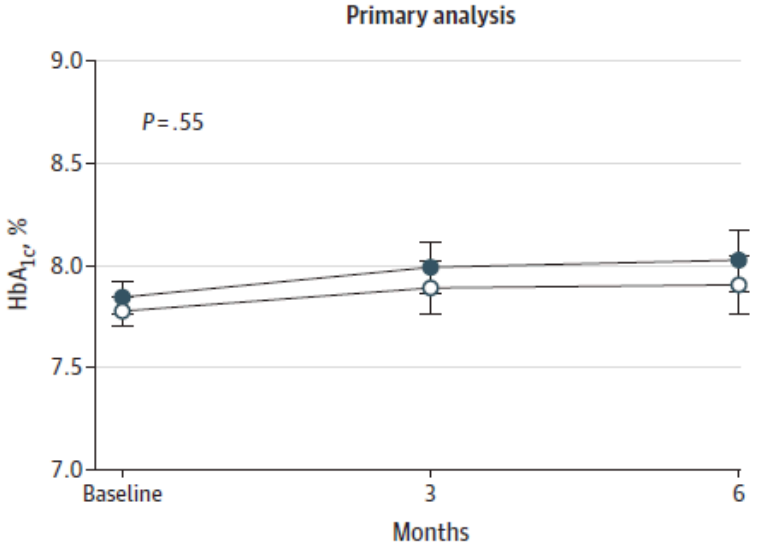


JAMA. 2013; 310(23):2523-2532.doi:10.1001/jama.2013.282431

Results

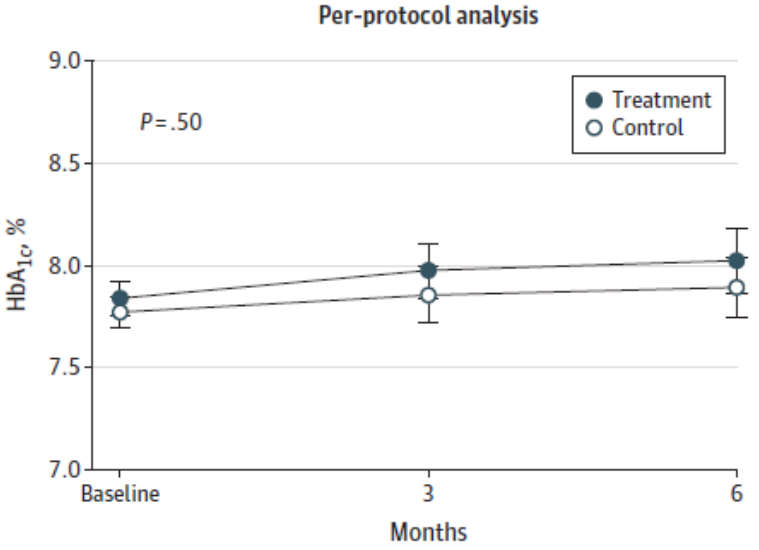
- Futility analysis was planned after the first 300 participants completed the 6-month visit
- Based on this analysis the Data Safety Monitoring Board (DSMB) recommended ending recruitment and completion of enrolled participants
- And the outcome was…

HbA1c at baseline and follow-up



No. of participants

Treatment	257	257	257
Control	257	257	257



No. of participants

Treatment	240	233	240
Control	235	228	235

JAMA. 2013; 310(23):2523– 2532

Summary of HbA1c Results

- No differences in HbA_{1c} change were observed between the treatment and control groups
- HbA_{1c} values increased slightly in both groups over the 6-month period ~0.1%
- Findings were similar in the preliminary and the per-protocol analysis

Conclusions

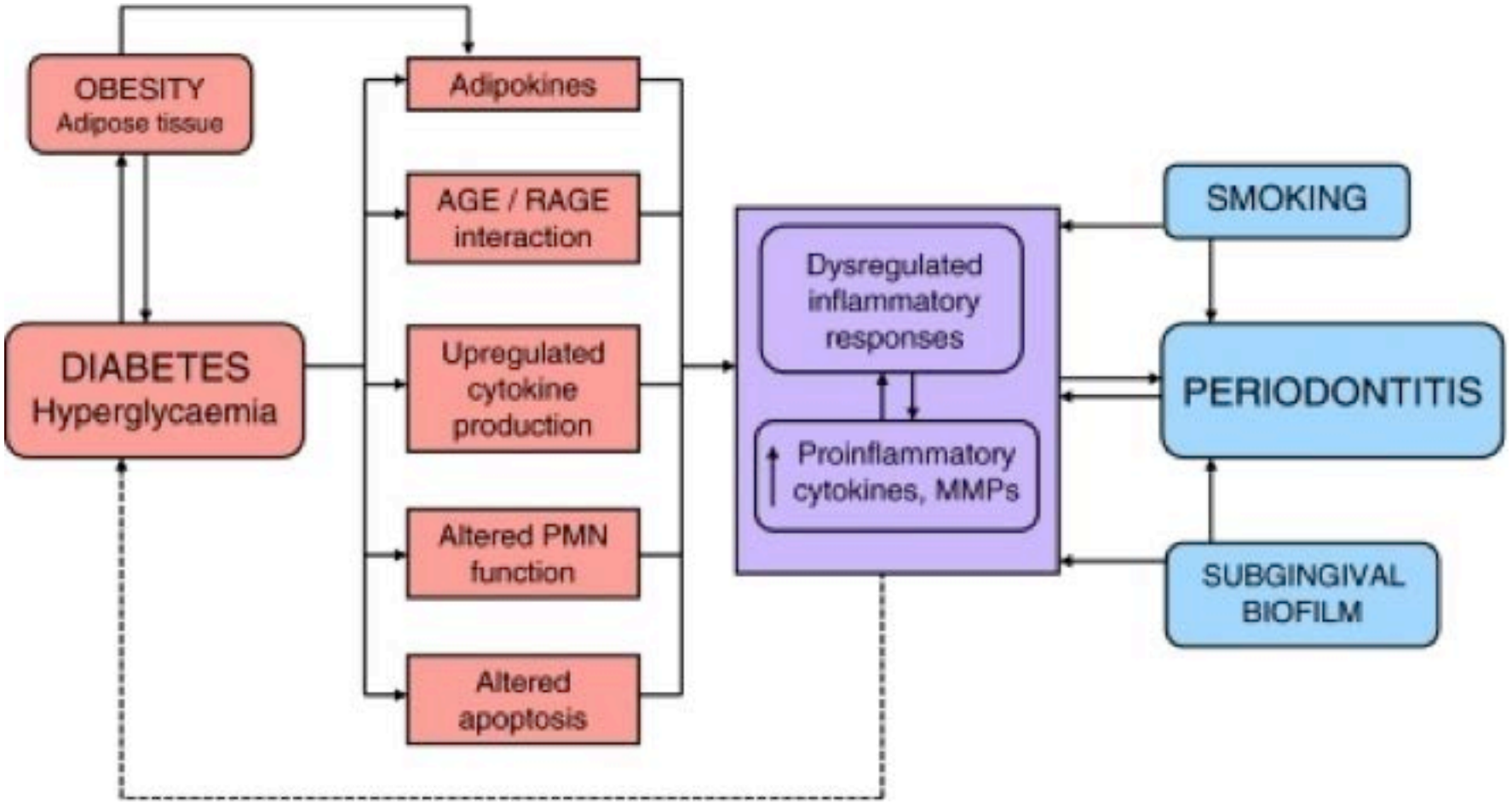
- This multi-centered randomized clinical trial of non-surgical periodontal treatment for participants with T2DM and chronic periodontitis
  - *did not demonstrate a benefit to measures of glycemic control*
- In a population with moderately controlled diabetes and moderate to severe periodontitis
  - *Non-surgical periodontal therapy did not influence diabetes management*
    - *regardless of age, gender, ethnicity, diabetes related factors, medication use or other factors studied*

Systemic effects of periodontitis treatment in patients with type 2 diabetes: a 12 month, single-centre, investigator-masked, randomized trial

- 264 patients with T2DM and moderate to severe periodontitis
- Randomly assigned to intensive (IPT) or control treatment (CPT)
- After adjusting for baseline HbAa1c, age, sex, ethnicity, smoking status, duration of DM, and BMI: HbA1c ws 0.6% lower in the IPT group when compared to the CPT group

D'Aiuto F, et. al. *Lancet Diabetes Endocrinol* (2018) 6:954-65

Diabetes and Periodontitis



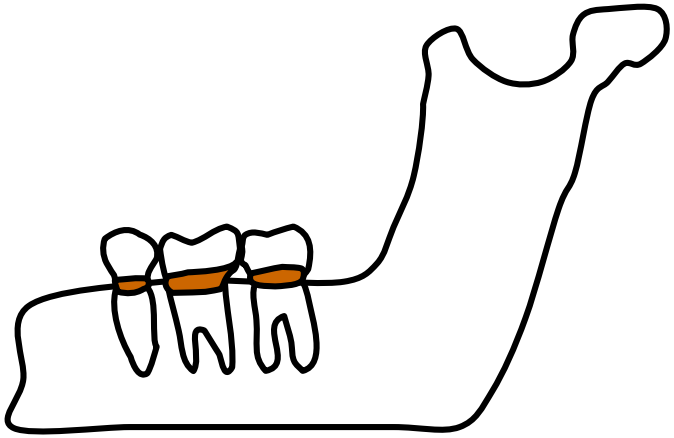
Summary/My Thoughts

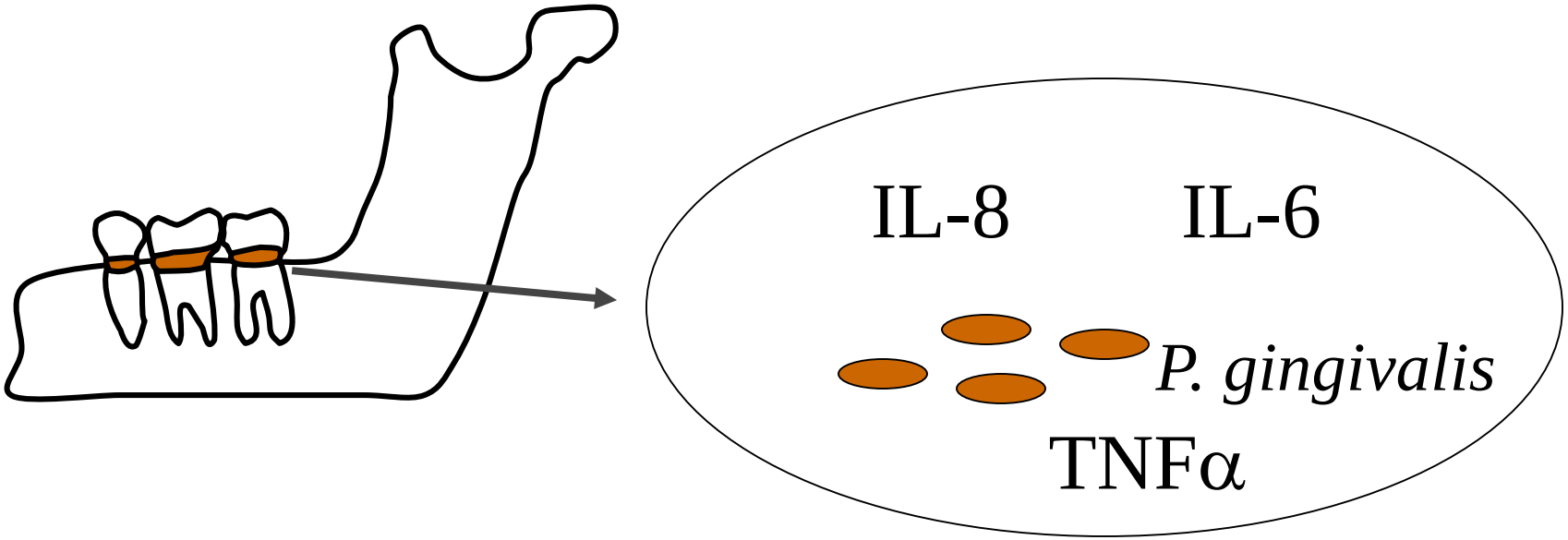
- Studies have consistently linked poor glycemic control in both type 1 and 2 diabetes with periodontitis
- Treatment of periodontitis may help control blood glucose levels in the more severe forms of the disease
- *Oral health care should be part of comprehensive diabetes care – addition of oral evaluation to Oregon Health Plan coordinated care organizations (CCO 2.0)*

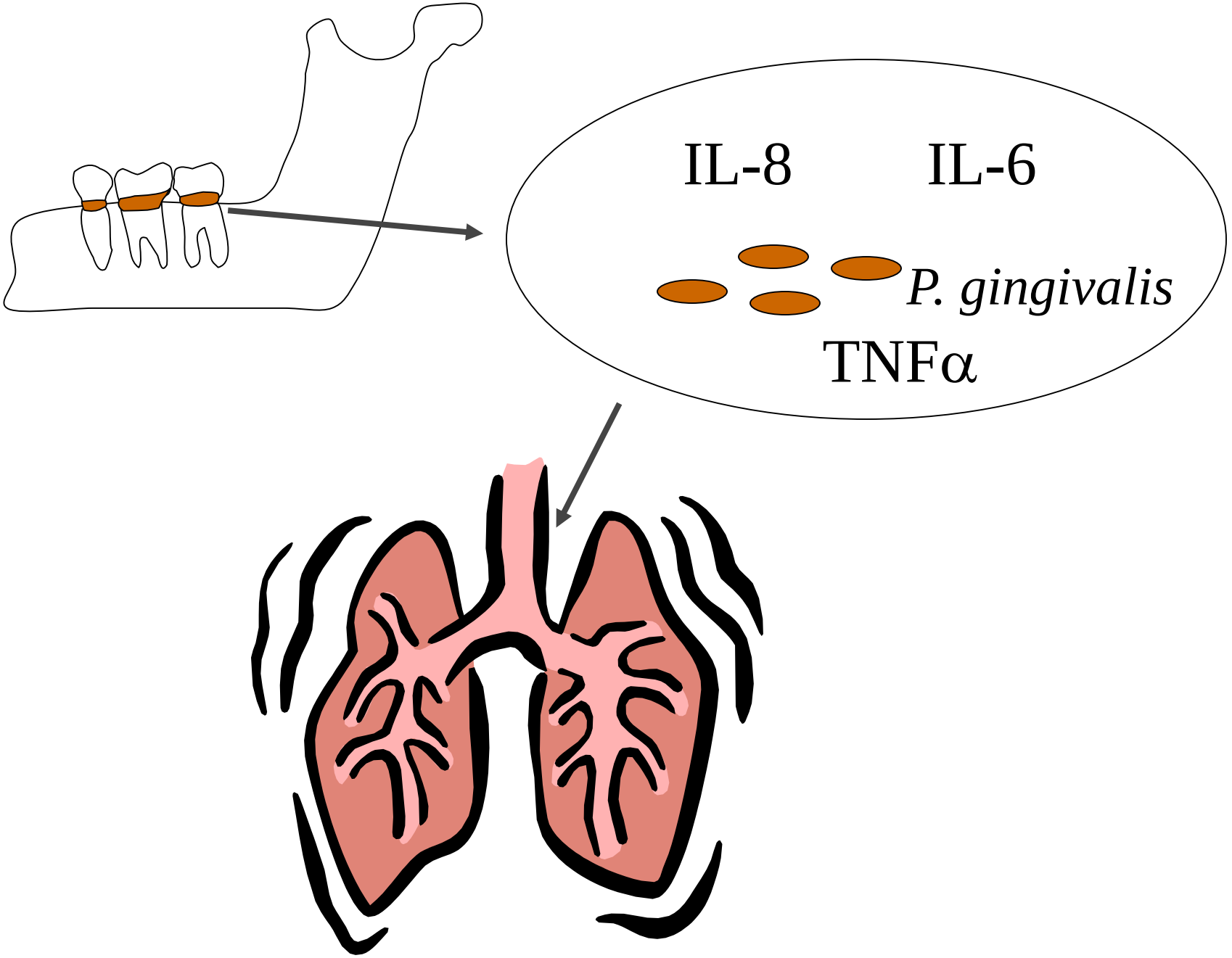
Periodontal and Respiratory Diseases

Respiratory diseases

- Lower respiratory infections third leading cause of death in 1990 (4.3 million)
- Chronic obstructive pulmonary disease sixth cause of death (2.2 million)
- Pneumonia and influenza




IL-8
IL-6
P. gingivalis
TNFα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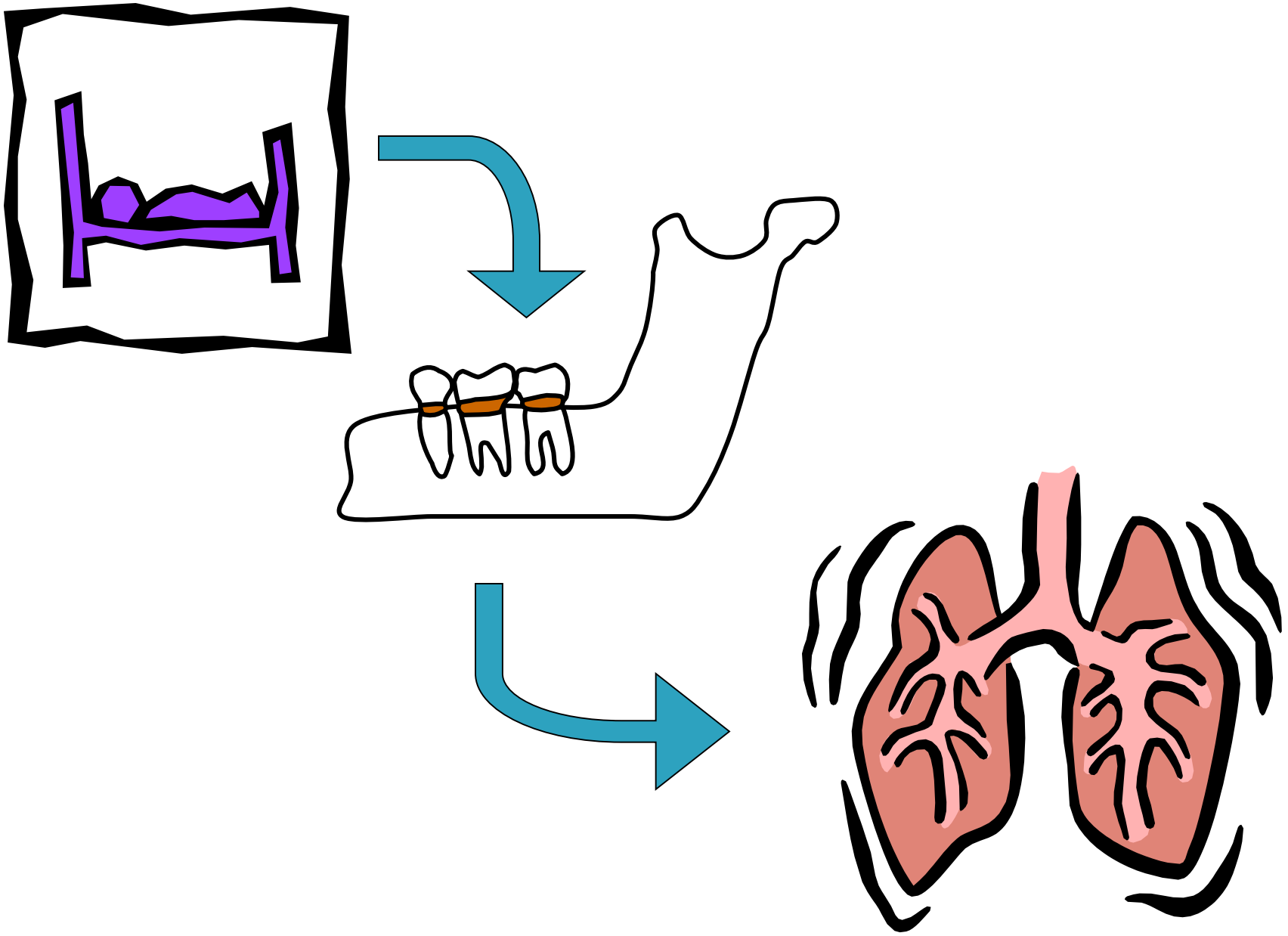


Oral anaerobes

- *Porphyromonas gingivalis*
- *Bacteroides oralis*
- *Eikenella corrodens*
- *Fusobacterium nucleatum*
- *A. actinomycetemcomitans*

Pathogens in dental plaque linked to pneumonia in elders (*Chest* 2004)

- 49 nursing home residents who were admitted to the ICU and required a respirator
- Of the 49 patients, 14 developed pneumonia including 10 from the respiratory pathogen group
- Fluid samples showed that of the 13 pathogens isolated from the patients' lungs, nine were genetically identical to pathogens recovered from the patients' dental plaque samples

Mechanisms linking periodontal disease to COPD

Periodontal disease may alter environmental conditions to permit mucosal colonization and infection by respiratory pathogens (Scannapieco, *J Perio*, 1999)

Treatment Considerations

- Oral hygiene education of medical and support staff within chronic care facilities
- Chlorhexidine (0.12%) rinses

Health Aging and Body Composition (Health ABC) Study (Katancik, et al. 2005)

- 3,075 participants enrolled at baseline in the Health ABC study
- 1,843 presented for an oral examination
- 1,171 participants receiving the complete periodontal probing examination, 1,053 had complete data available on all study variables

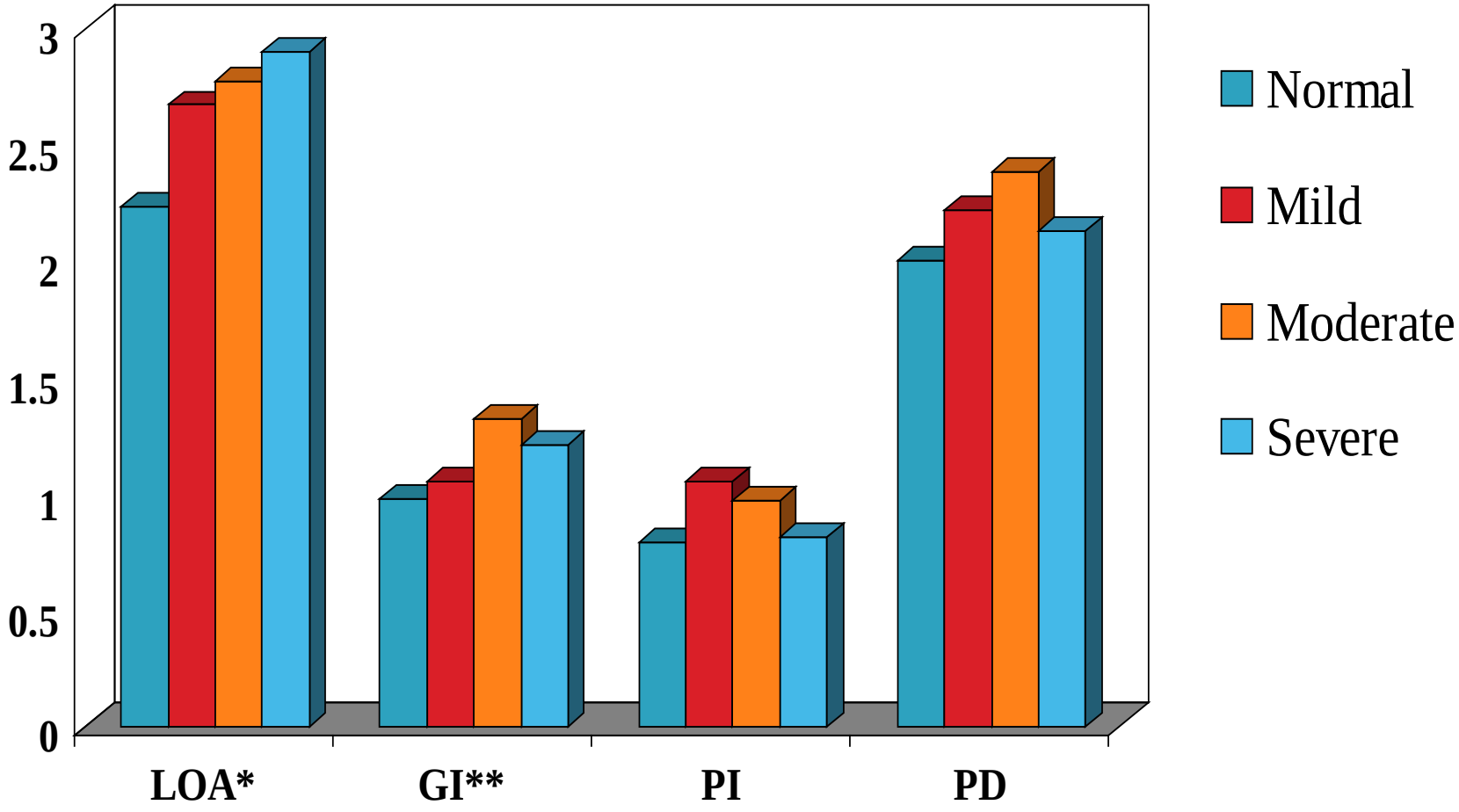
Oral Examination

- soft tissue exam
- dental exam
- periodontal probing
- microbial assessment (BANA)

Measures of Airway Obstruction

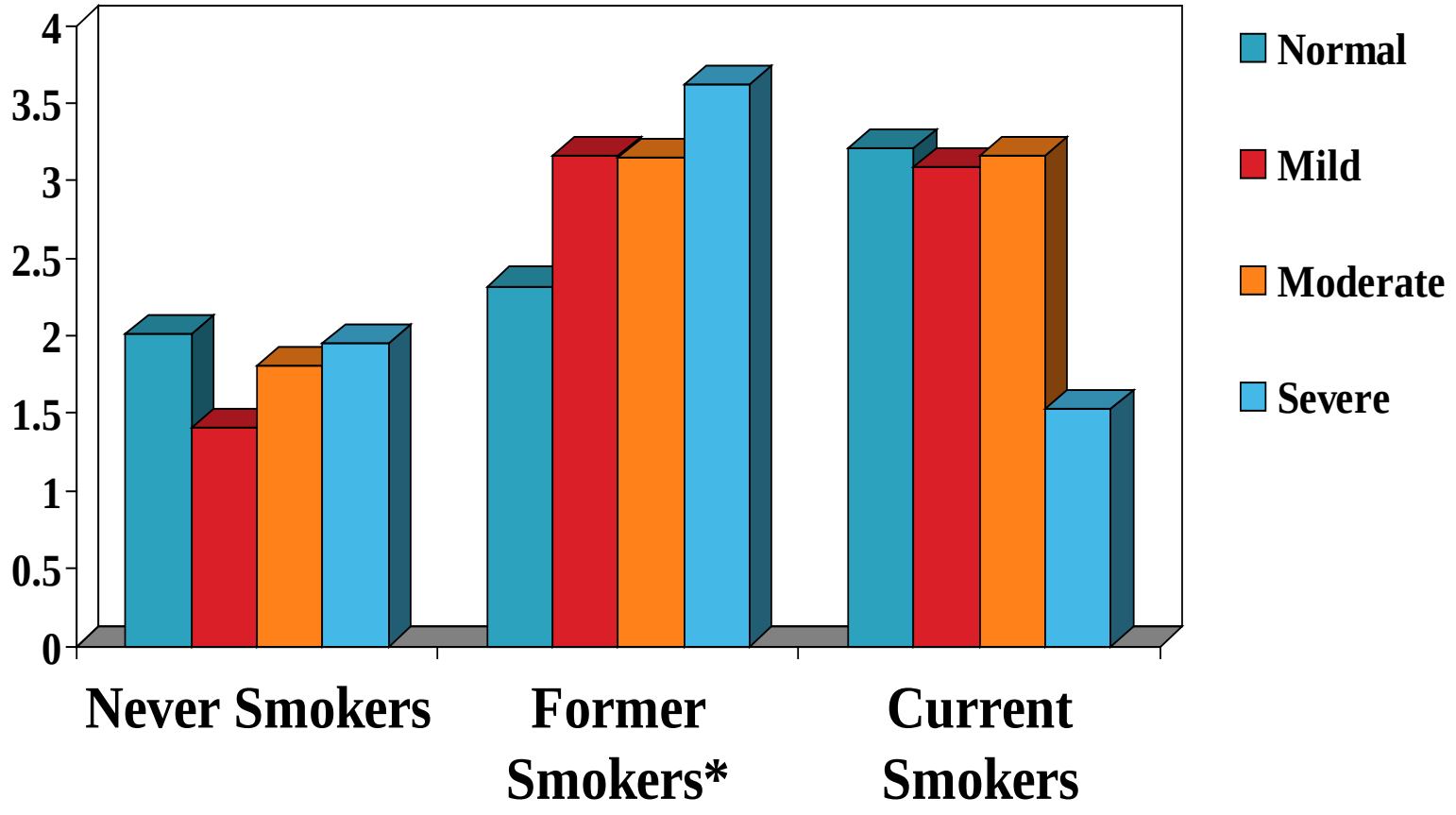
- Baseline based on FEV_1 / FVC ratio
- Severity based on degree of FEV_1 reduction

Periodontal Indices According to Level of Obstructive Disease



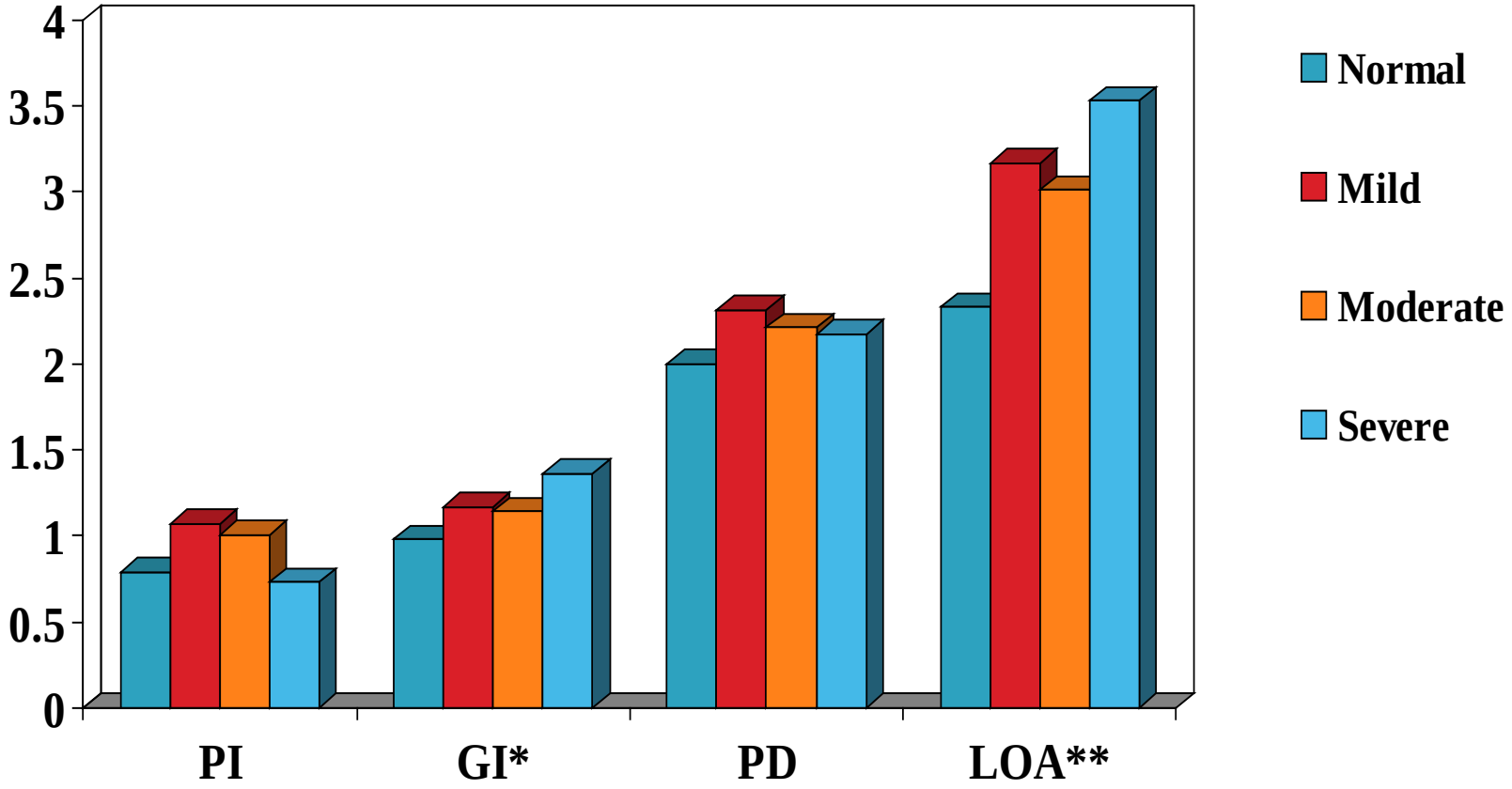
***p = 0.007 **p = 0.031 (adjusted for age, race, gender, site)**

Loss of Attachment According to Smoking Status and Level of Obstructive Disease



*p < 0.001 (adjusted for pack years, age, race, gender, and site)

Former Smokers by Level of Obstructive Disease



*p = 0.032 **p < 0.001 (Adjusted for pack years, age, race, gender, site)

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Questions?