Prediabetes and Oral Health: Epidemiologic and Clinical Perspectives

Prediabetes and Oral Health Conference

Maryland Department of Health and Mental Hygiene
Center for Chronic Disease Prevention and Control
in collaboration with the Office of Oral Health
Clarksville, MD: June 26, 2015

UCSF
University of California
San Francisco

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Overview

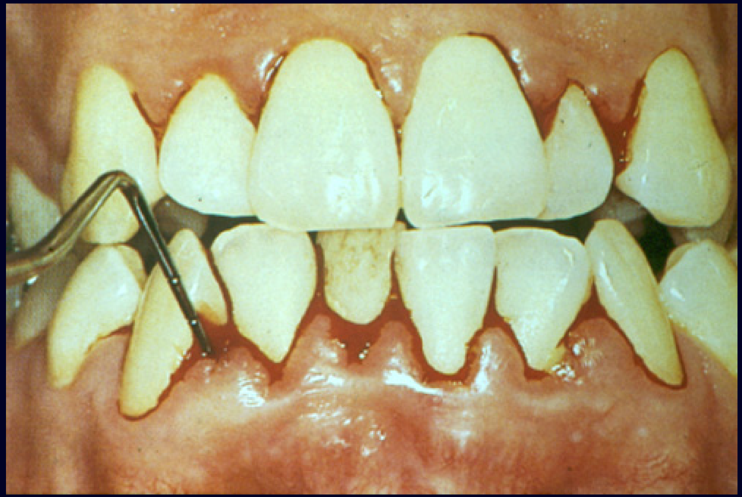
- Evidence for adverse effects of diabetes and prediabetes on oral health
- Evidence (conceptual model and empirical evidence) for effects of periodontal infection on:
  - insulin resistance
  - glycemic control
  - diabetes complications
  - diabetes and prediabetes incidence

Overview, cont.

- Role of dental care providers in detection of undiagnosed prediabetes and diabetes
- Action steps for dental care and medical care providers in addressing oral health within the context of prediabetes and diabetes

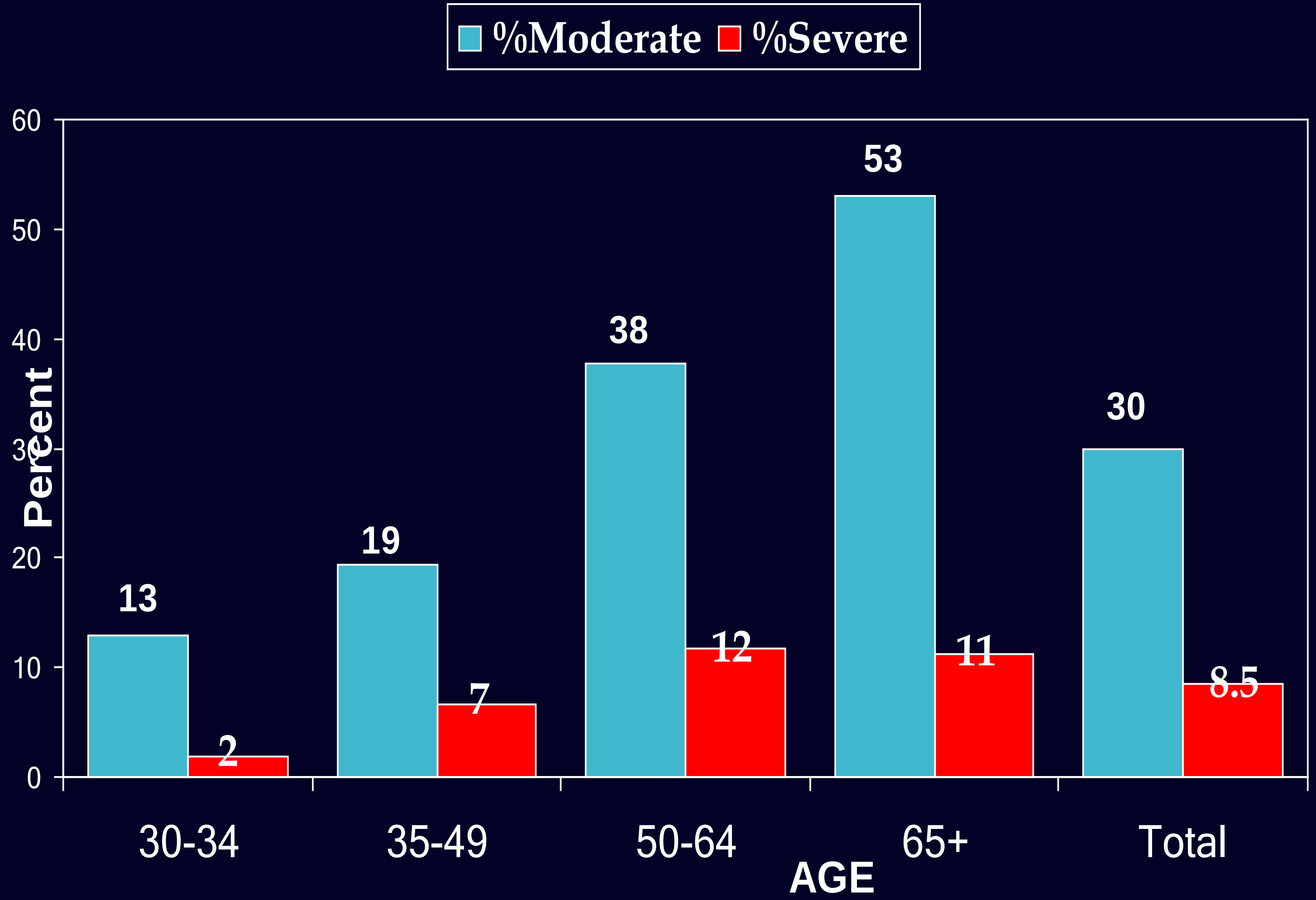
Periodontal disease

- 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
- Chronic source of systemic challenge
  - Bacteria and bacterial products (e.g. LPS)
  - Inflammatory mediators



Periodontal health and disease

Prevalence of moderate or severe periodontitis in US adults: NHANES 2009-10



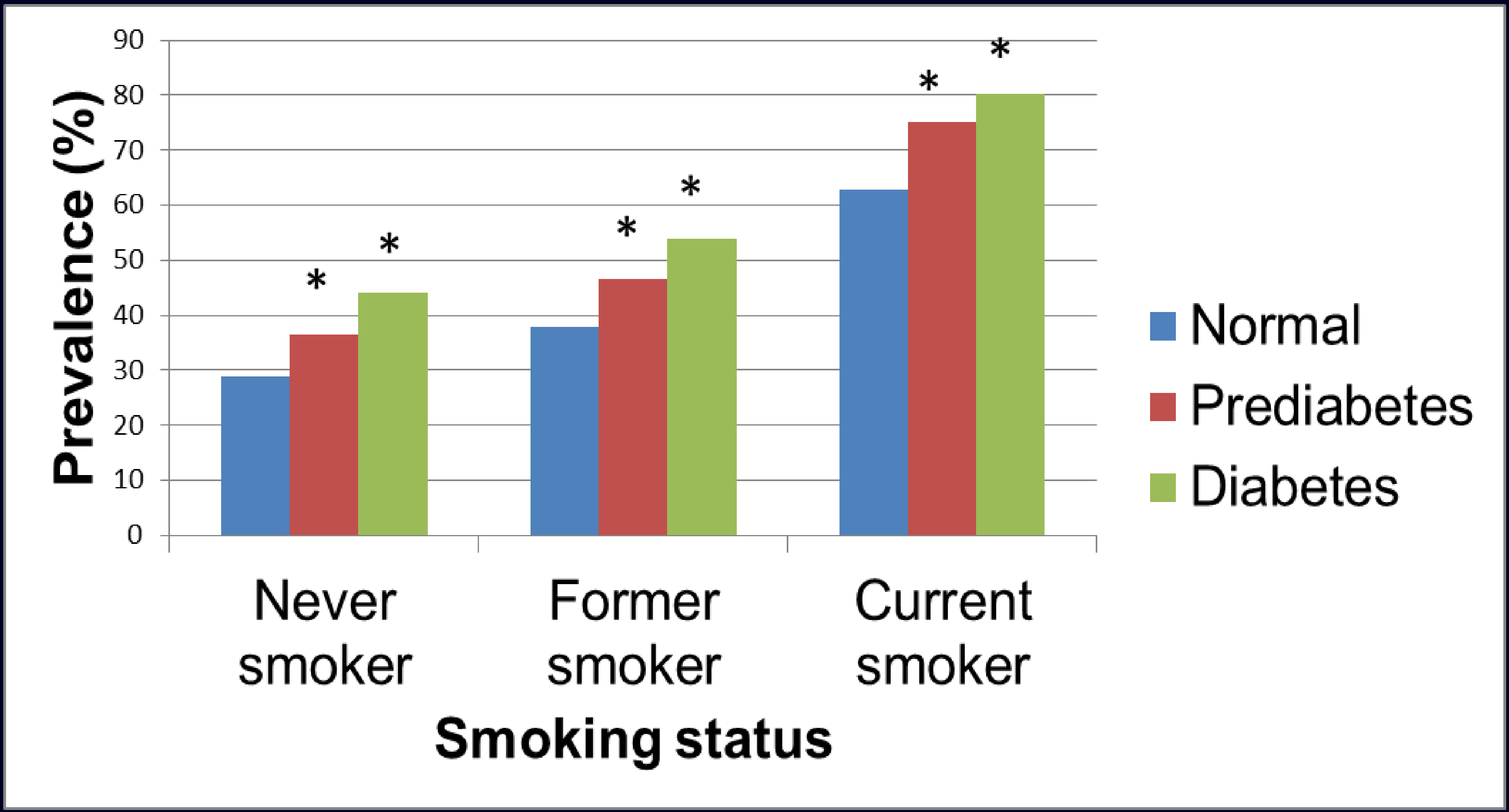
Moderate Perio:
2+ teeth with
AL ≥4 mm OR
2+ teeth with
PD ≥ 5mm at
interprox. sites

Severe Perio:
2+ teeth with
AL ≥6 mm AND
1+ teeth with
PD ≥ 5mm at
interprox. sites

Source: Eke et. al., J Dent Res, 2012

Diabetes and prediabetes: adverse effects on periodontal health

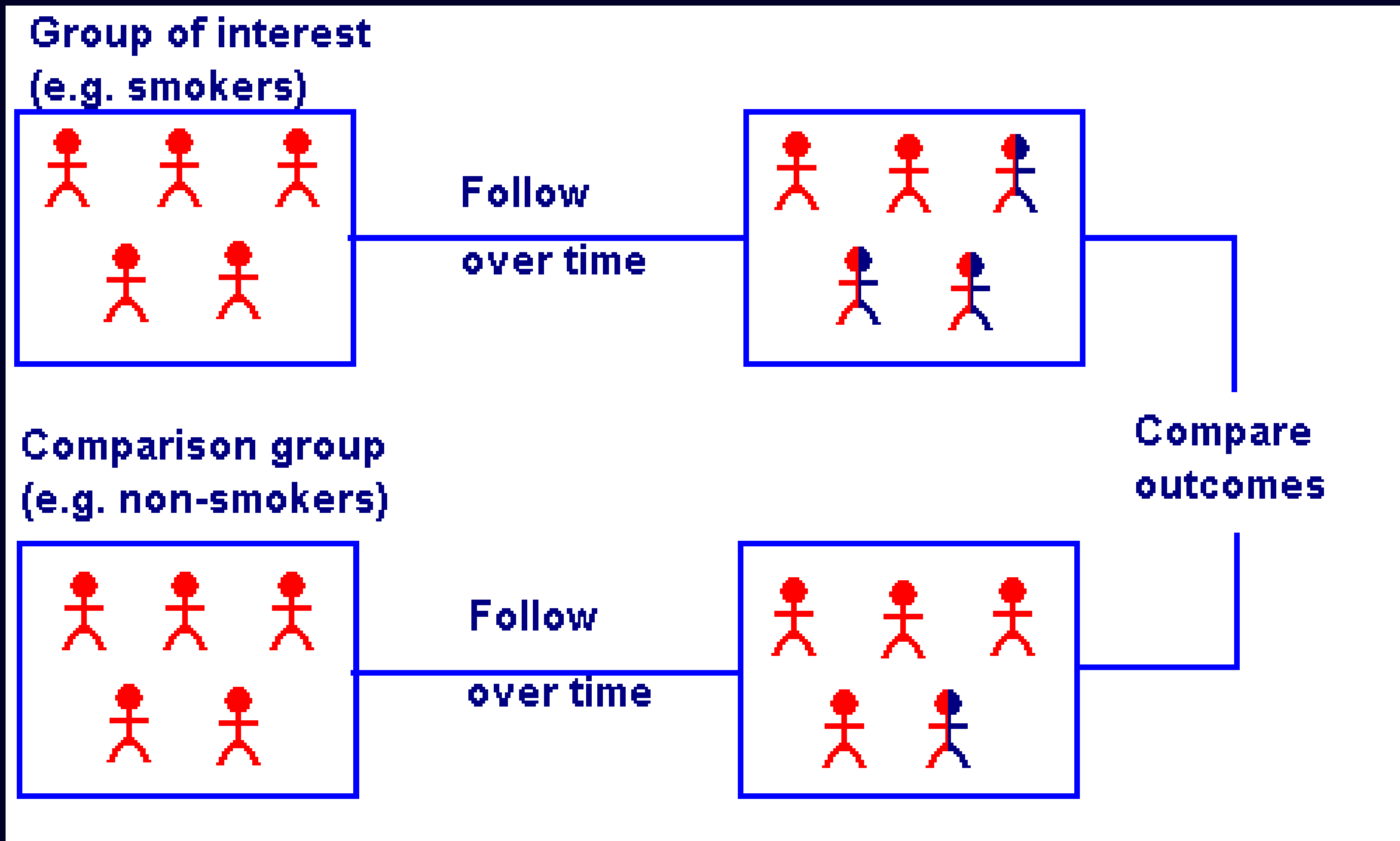
Age-standardized prevalence of moderate or severe periodontal disease by diabetes status and smoking status, US adults ages 30+. NHANES 2009-2012



Diabetes: adverse effects on periodontal health

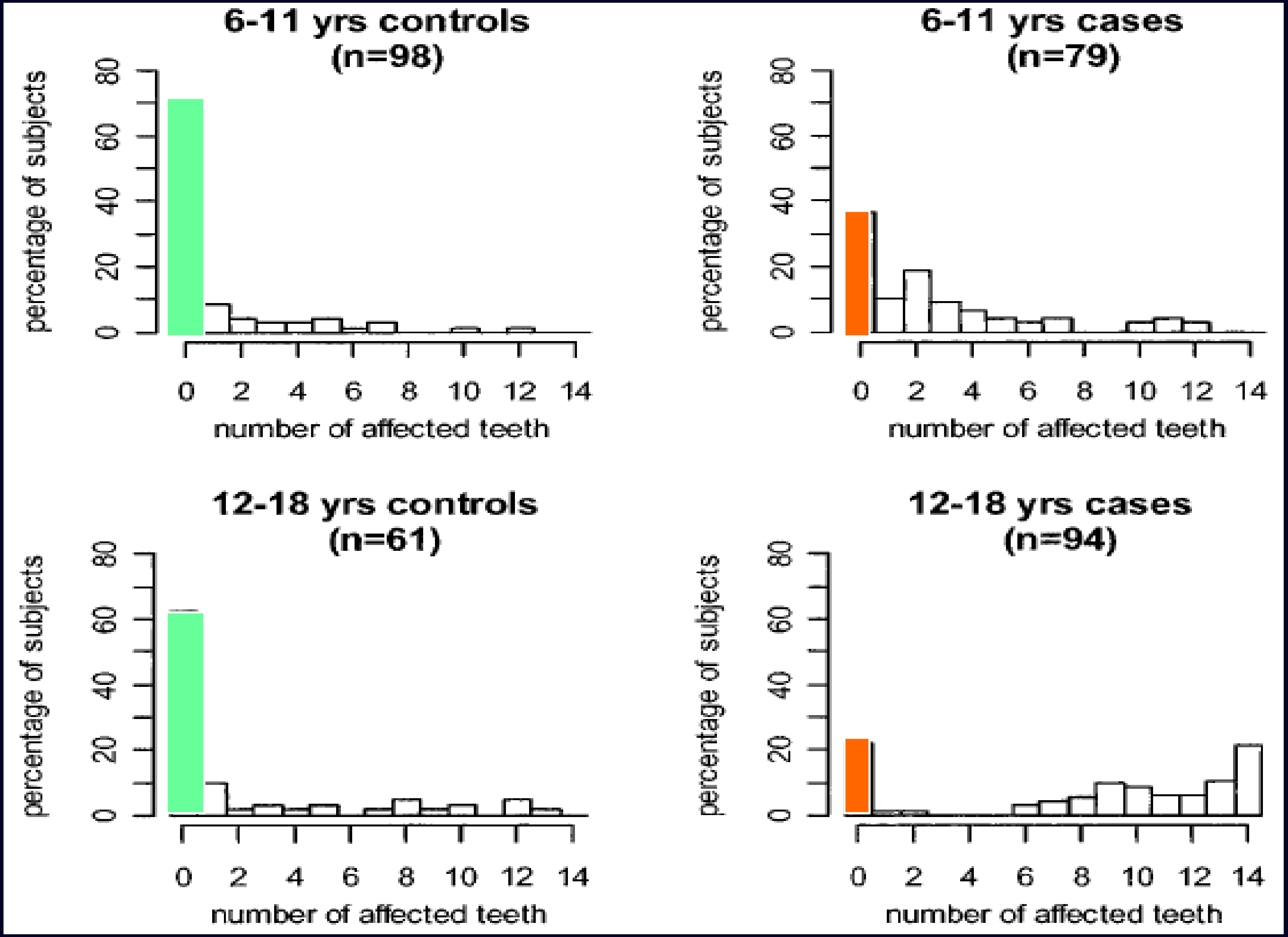
- Type 1 DM: children, adults
- Type 2 DM: adults, especially poorly controlled
- Gestational diabetes

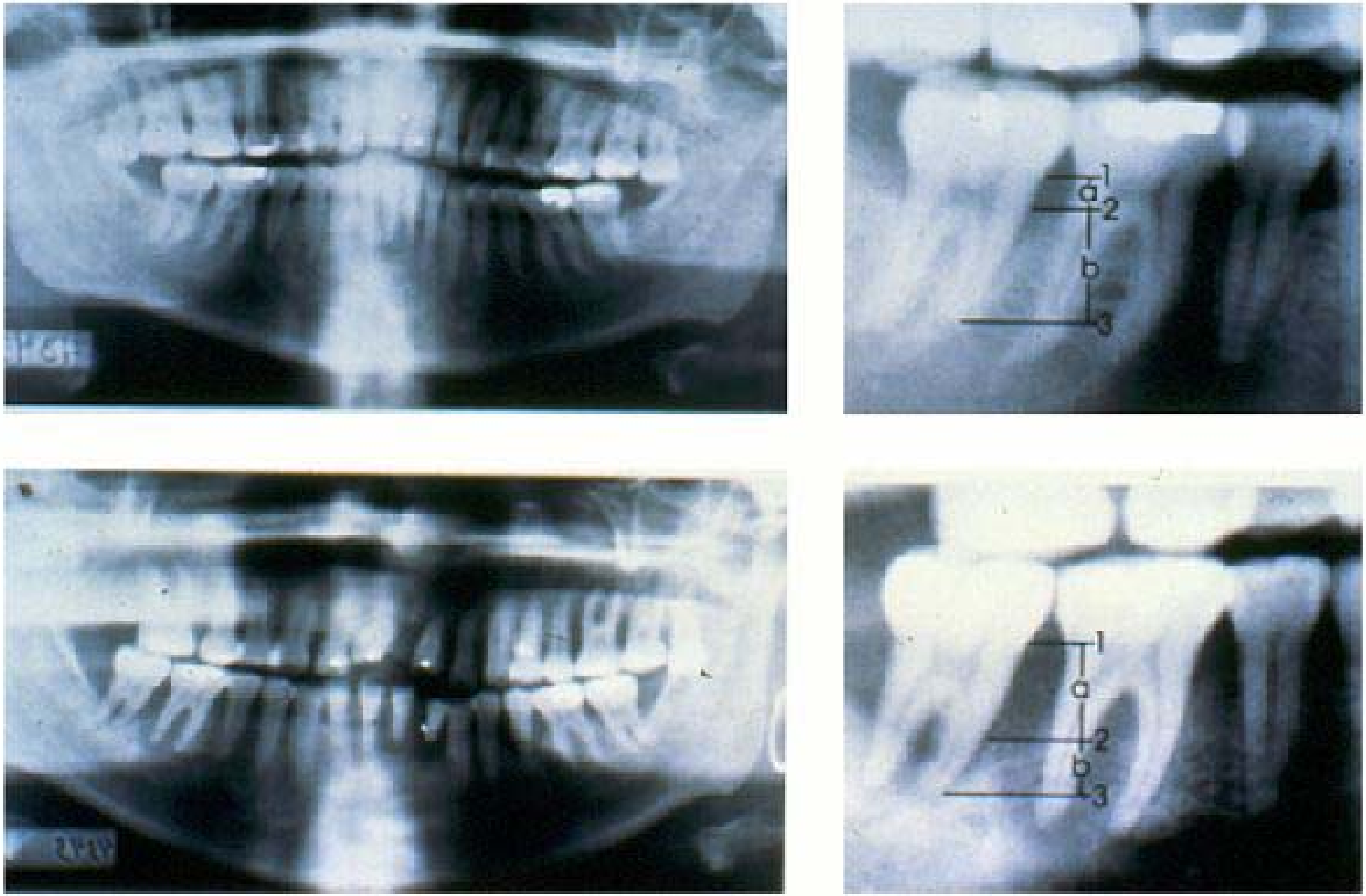
Cohort Studies (Prospective studies)



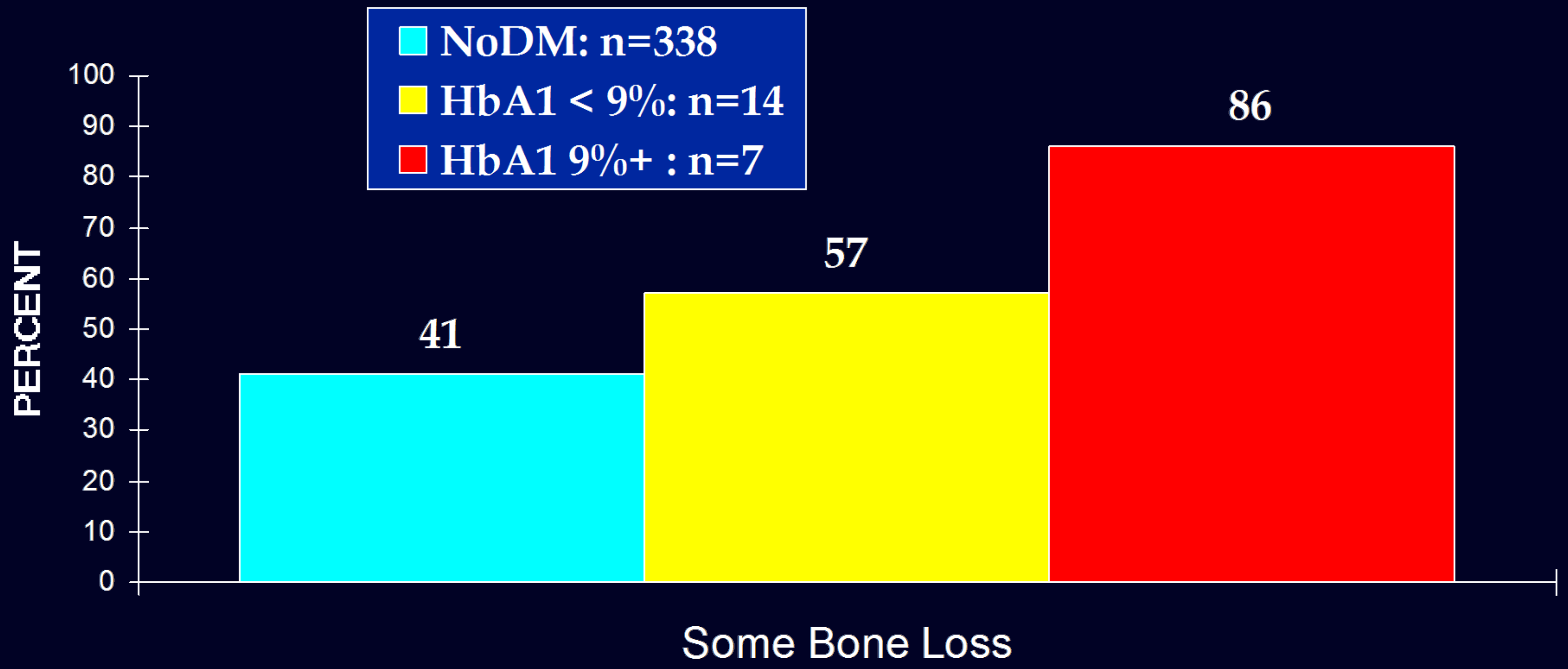
Source SUNY-http://library.downstate.edu/EBM2/2400.htm

% Children and adolescents having NO sites with periodontal attachment loss ≥ 2mm. (Lalla E et al. 2006)




1
a
2
b
3
1
a
2
b
3

Incidence of Alveolar Bone Loss after ~2 Years Follow-up in the Pima Indians



Source: Taylor et al., 1998

Five-year change in attachment loss by diabetes status

Adjusted for: age, gender smoking, WHR, and education.

Source: Demmer et. al., 2012, Diabetes Care

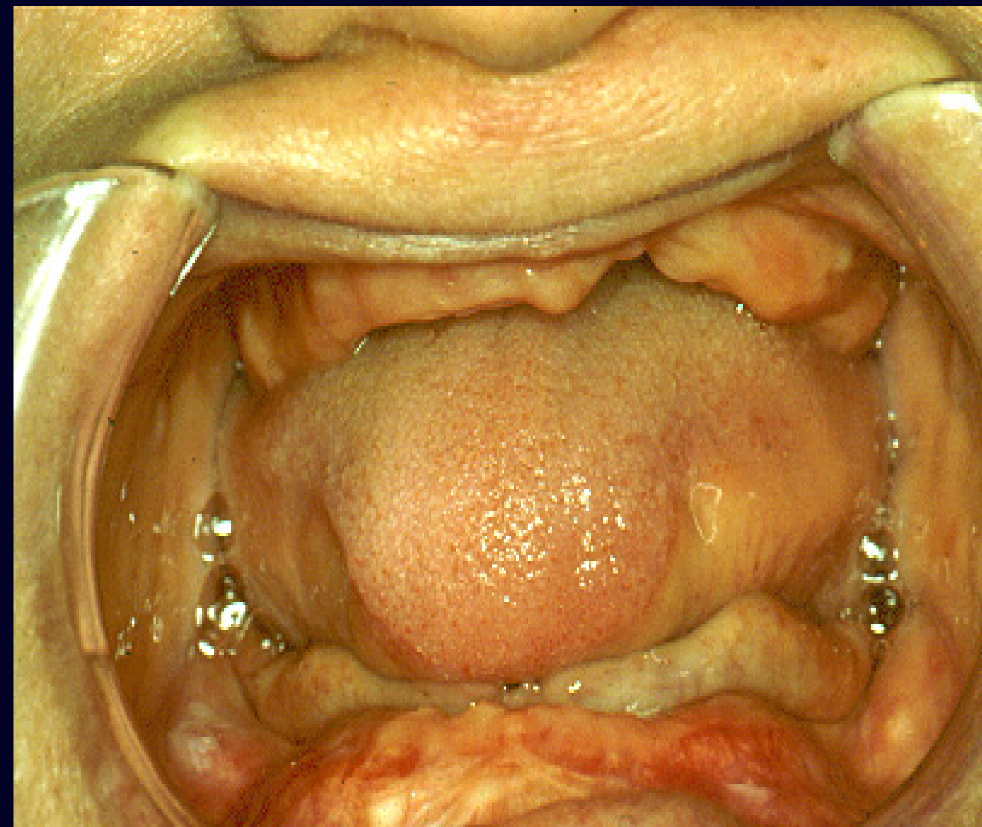
Gestational diabetes mellitus and more prevelant periodontitis

Authors	Year	Location	GDM PD Prev	NO_GDM PD Prev	Odds Ratio	95%_CI
Chokwiriyachit A, et al.	2013	Thailand	50%	26%	3.0	1.2, 7.6
Xiong X, et al.	2009	U.S.	77%	57%	2.6	1.1, 6.1
Novak KF, et al.	2006	U.S.	9.0-31.0%	4.8-11.6%	8.0	P<0.05
Xiong X, et al.	2006	U.S.	29-45%	14%	9.1	P<0.05
Esteves L, et al.	2013	Brazil	40%	46.30%	0.7	P>0.05

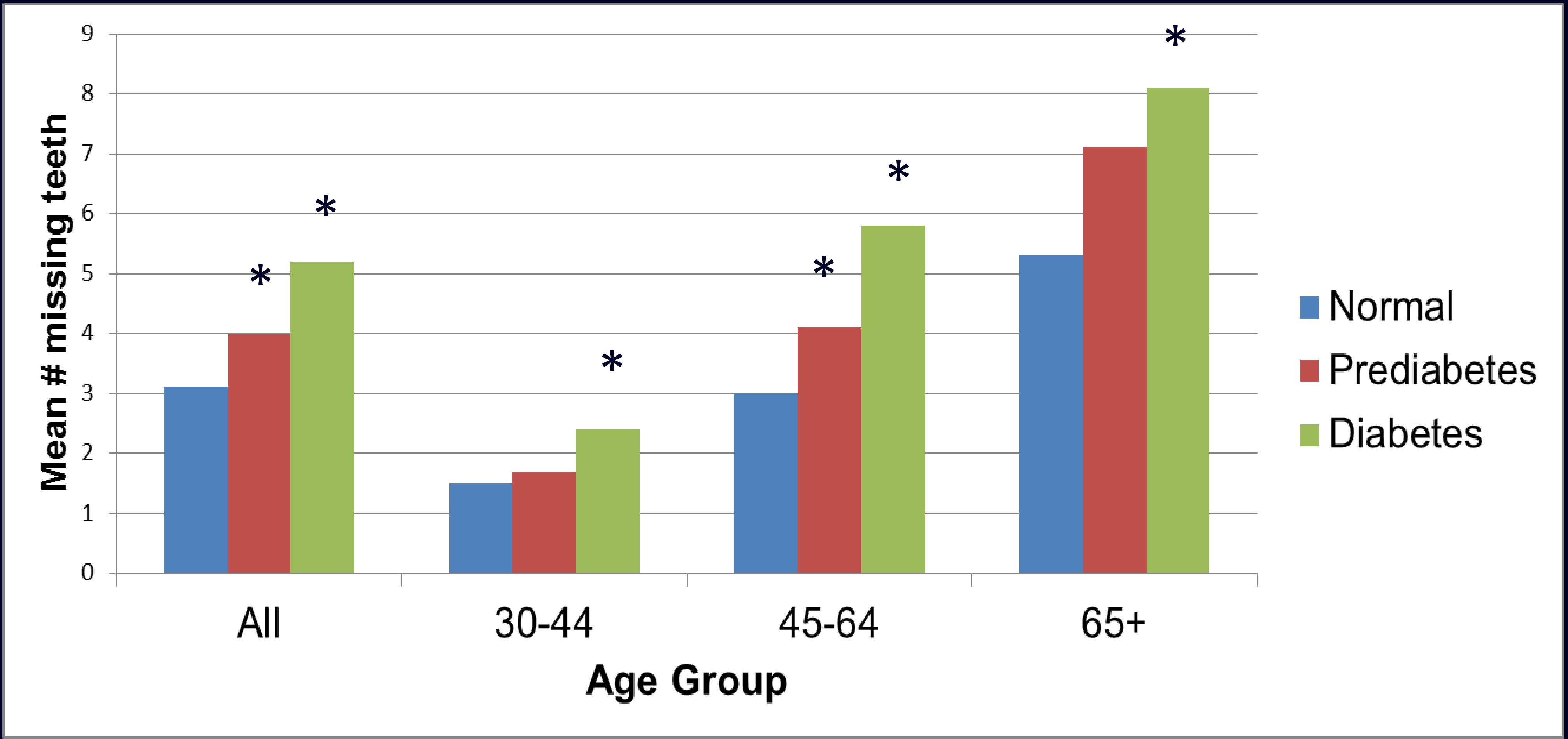
Status of the evidence for adverse effects of diabetes on periodontal health: 1967 to 2011

Study design	**Total # Studies +**
Cohort study	8/9
Cross-sectional	93/106
Total	101/115

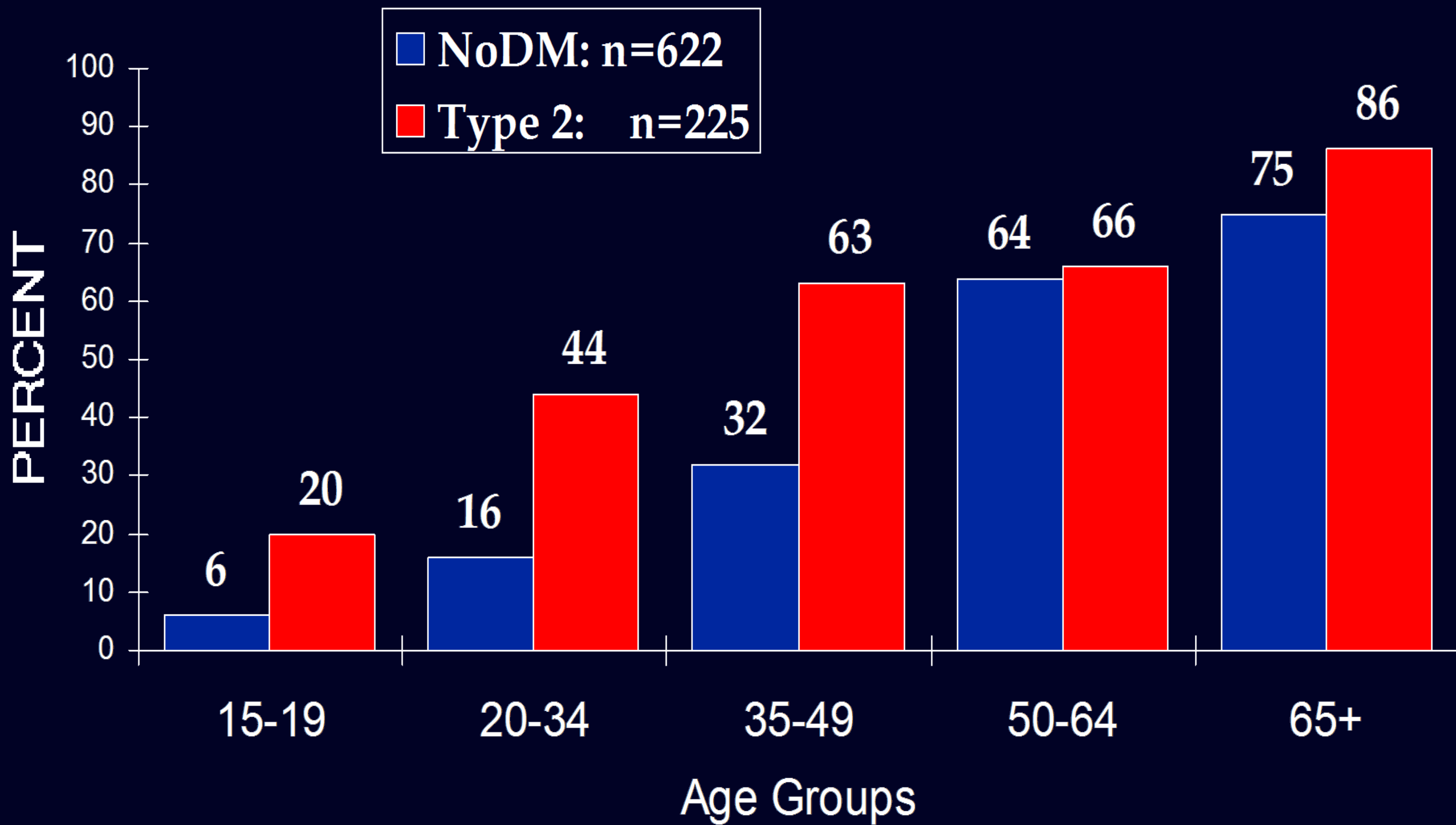
Diabetes, prediabetes and tooth loss



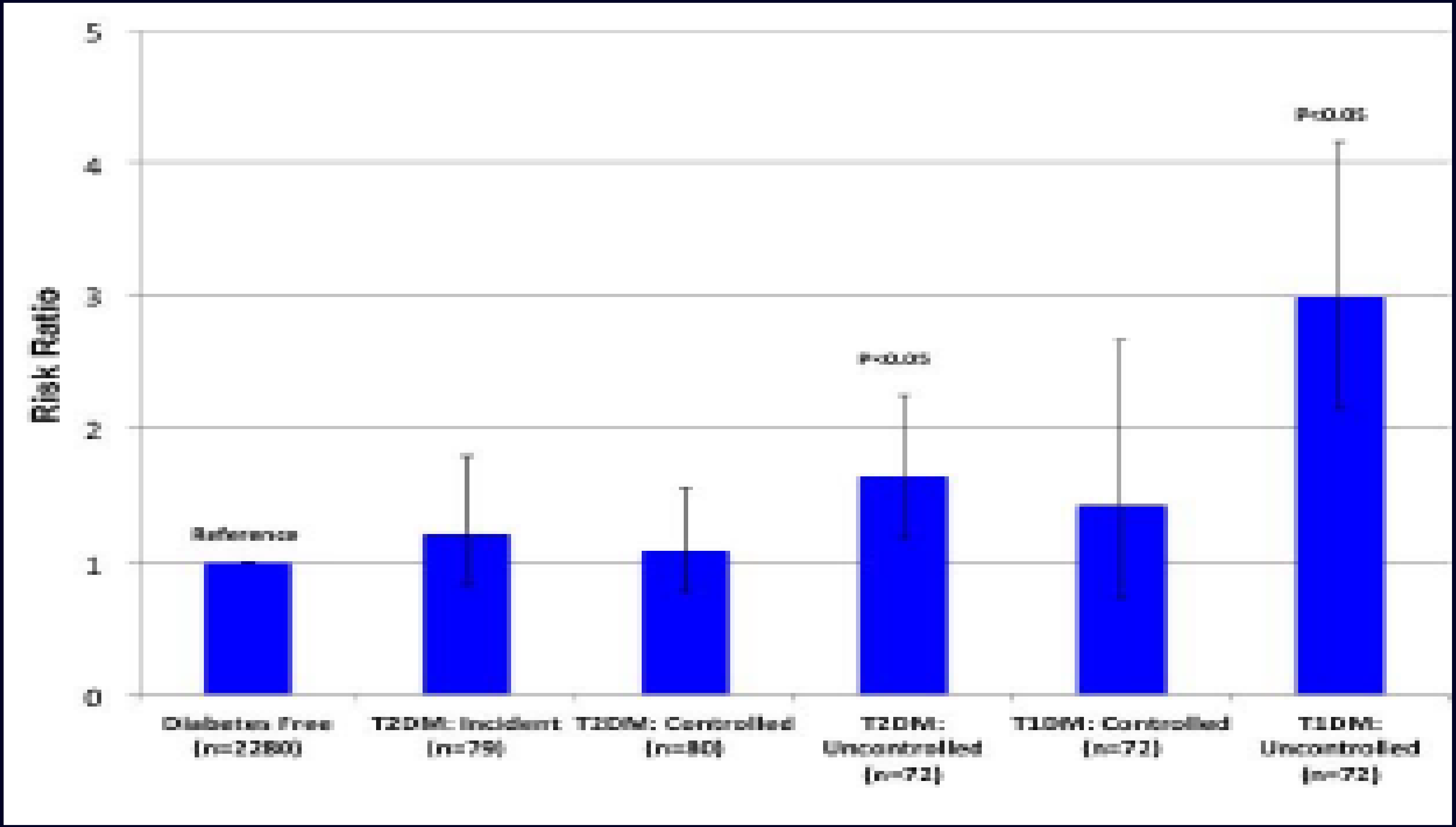
Mean number of missing teeth by diabetes status and age, US adults ages 30+. NHANES 2009-2012



Partial tooth loss in the Pima Indians



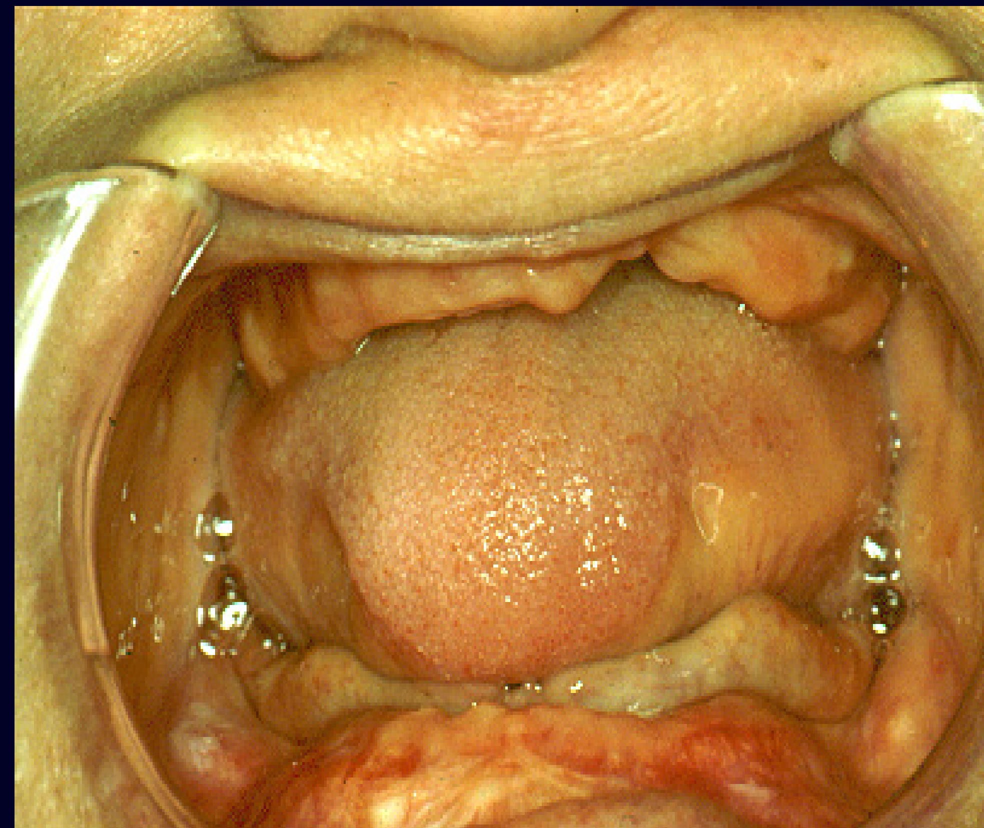
Risk for losing >1 tooth after 5-years follow-up: Study of Health in Pomerania (Germany) by diabetes status



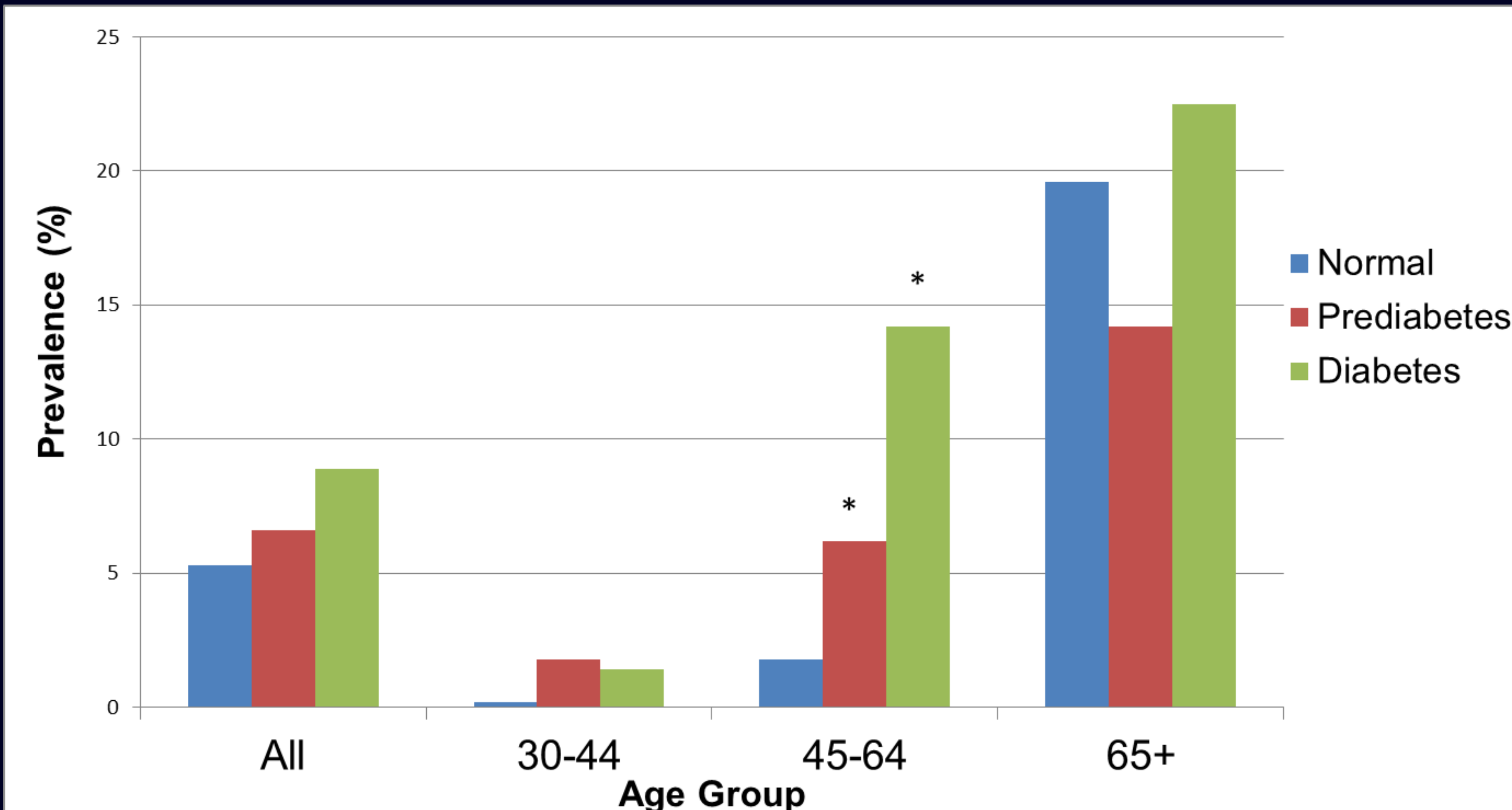
Adjusted for: age, gender smoking, WHR, and education.

Source: Demmer et. al., 2012, Diabetes Care

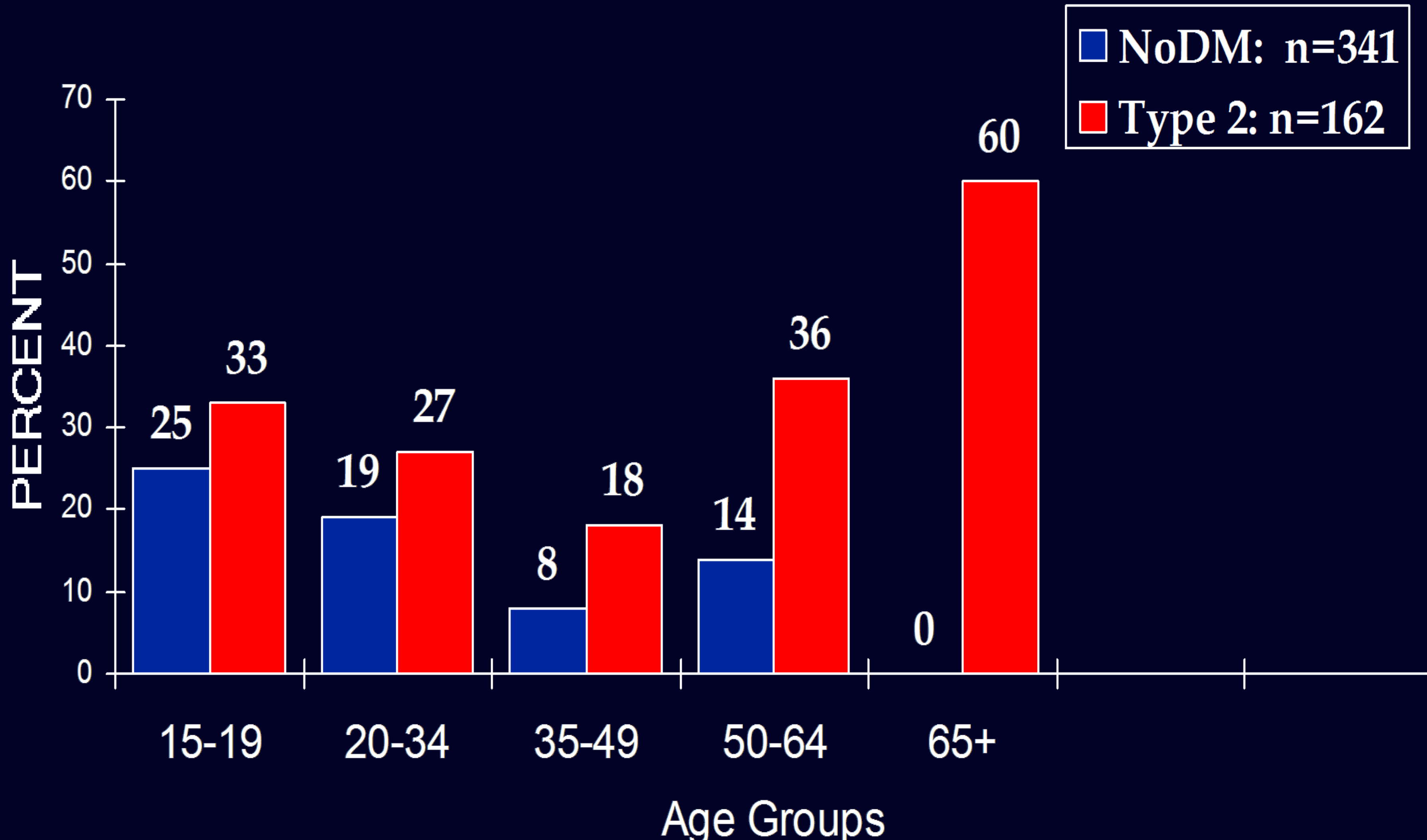
Diabetes, prediabetes and edentulism



Prevalence of edentulism by diabetes status and age: U.S. adults ages 30+ years, NHANES 2009-2012.



Diabetes and edentulism: Pima Indians

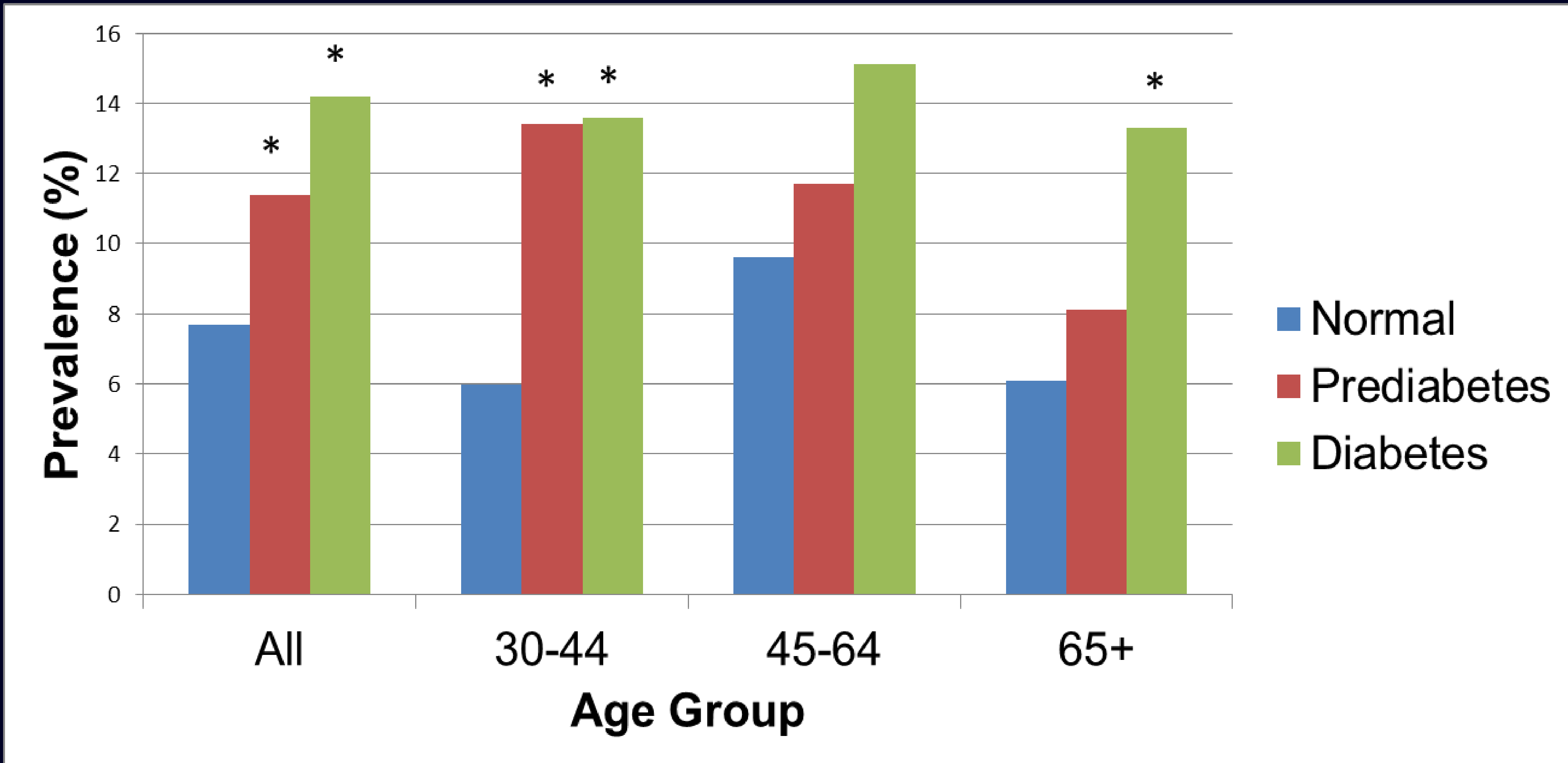


Diabetes, prediabetes and root caries

Root fragments

Source: Pereira, Ines, et. al. Rev Port Estomatol Med Dent Cir Maxilofac. 2014;55:110-4.

Prevalence of any root fragments by diabetes status and age: U.S. adults ages 30+ years, NHANES 2009-2012.



Periodontal Infection, Adverse Effects on:

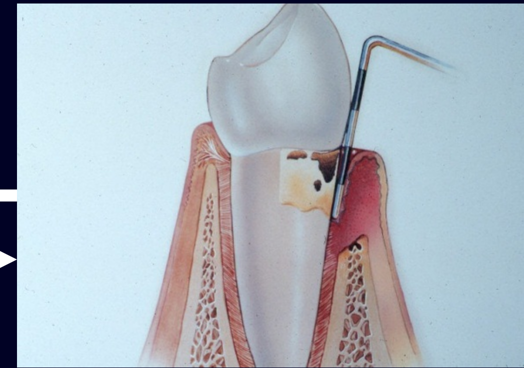
Glycemia in diabetes-free individuals

Diabetes outcomes

Periodontal Infection and Systemic Inflammatory Burden: Conceptual Model for Prediabetes and Diabetes

- Biologic pathway to help us think about a bi-directional relationship

Chronic inflammation
Visceral obesity



Il-1β
Il-6

TNFα

Proinflammatory state
Chronic over-expression of cytokines

Pancreatic beta cell damage

Liver

Insulin resistance

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

IFG, IGT,
Diabetes
Glycem Ctrl

Conceptual Model: Adapted from Richard Donahue, 2001

EMPIRICAL EVIDENCE

Periodontitis and Insulin Resistance: Epidemiologic Evidence of an Association

Periodontal Infection **and Insulin Resistance**: Emerging Evidence (Demmer et al., 2012)

- Study design: cross sectional, NHANES, 1999 – 2004
- Population: U.S. adults (N=3,616), diabetes-free
- Exposure: Periodontal disease
  - Quartiles of mean probing pocket depth (PD)
  - CDC-AAP definition for no, mild, moderate, severe pdz
- Comparison group: a.Q1; b. no/mild periodontal disease
- Outcome: HOMA-IR (insulin resistance)
- Results: PD assoc. with HOMA-IR ≥75 (RR=1.24); CDC-AAP severe assoc. with HOMA-IR≥75 (RR 2.3)
  - Analysis adjusted for demographics, SES, smoking, physical activity, adiposity, hypertension, lipids, CRP, and WBC

Periodontal Infection, impaired fasting glucose, and impaired glucose tolerance: (Aora et al., 2014)

- Study design: cross sectional, NHANES, 2009 – 2010
- Population: U.S. adults (N=1165), diabetes-free
- Exposure: Periodontal disease (pdz)
  - ≥ 75th percentile for mean probing depth or attachment loss
  - CDC-AAP definition for no/mild *vs* moderate or severe pdz
- Comparison group: a.<75th Q; b. no/mild pdz
- Outcome: IGT, IFG
- Results and Concl.: Periodontal infection assoc with IGT
  - Severe pdz assoc. with IGT (OR: 1.93; [1.2, 3.2]);
  - Probing dpth ≥ 75th assoc. with IGT (OR: 2.05 [1.24,3.39]
    - Adjusted for sociodemographics, health behavior, adiposity

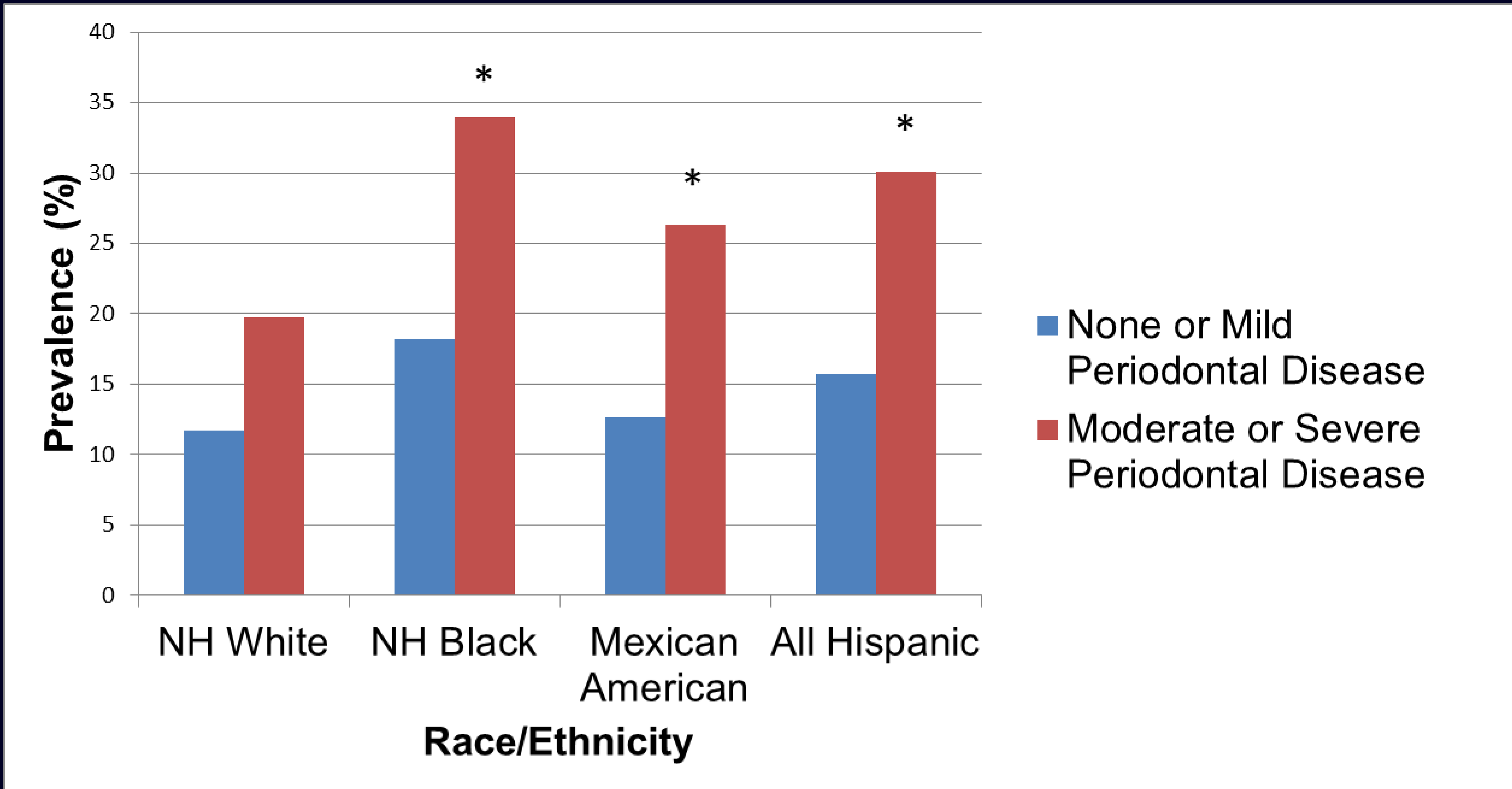
Periodontal Disease and dysglycemia development, but not diabetes

Study	N (Age)	#Years FU	Outcome
Demmer 2010 Germany	2,793 (20-81yr)	5yrs	HbA1c increase
Saito 2004 Japan	961 (40-79yr)	10yrs	HbA1c increase Glucose intolerance

Periodontal Infection Effect on Glycemic Control:

Observational Epidemiological Studies

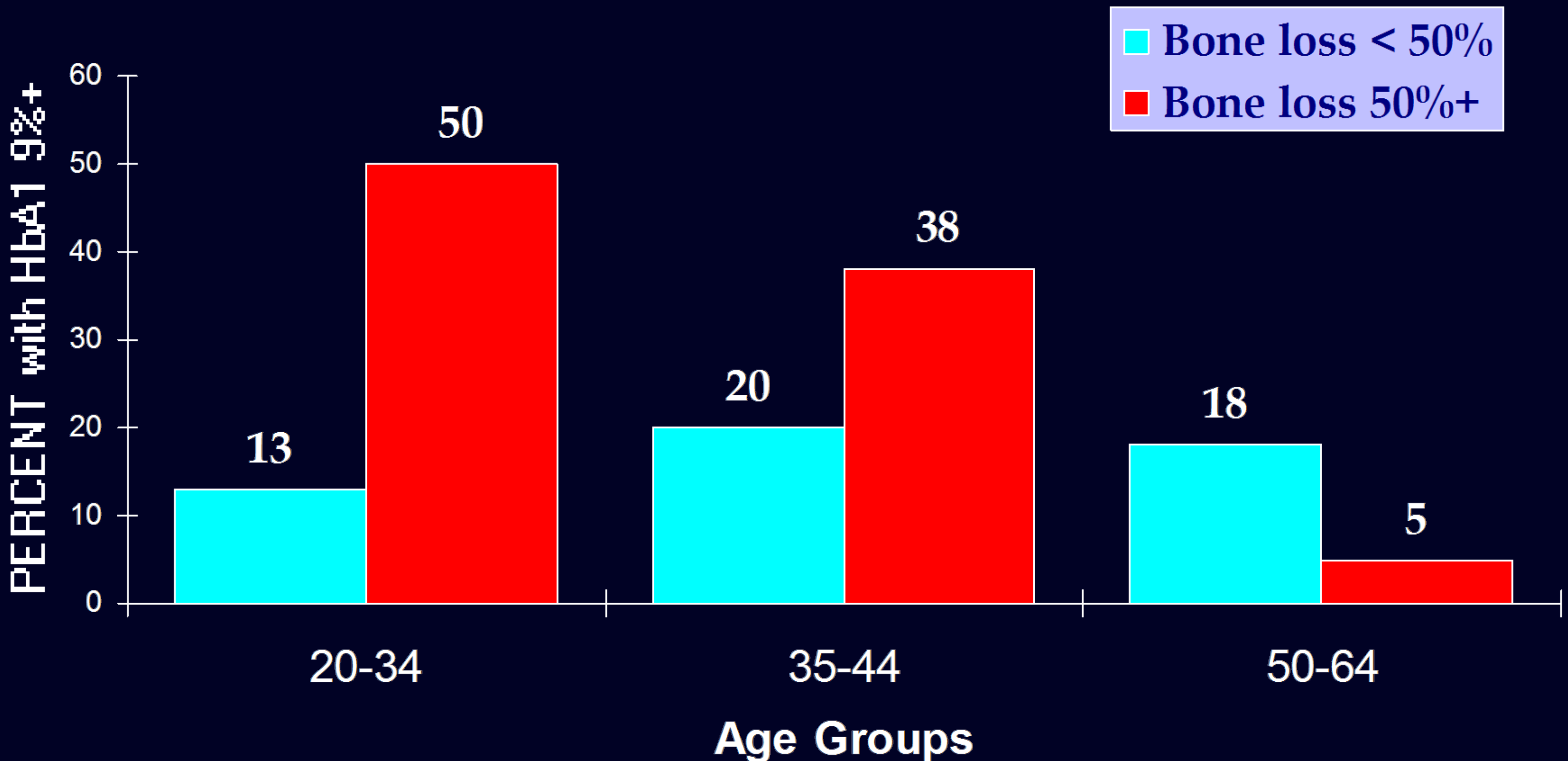
Age-standardized prevalence of A1c>8 by periodontal disease status and race/ethnicity: US adults ages 30+, NHANES 2009-2012.



Periodontal disease and poor glycemic control: epidemiologic evidence

- Population: Gila River Indian Community
- Ages: 18-67
- Dentate
- Baseline HbA1 <9%
- Periodontal status: Radiographic bone loss
- Follow-up: 88 at least 1 follow-up exam
  17 two follow-up exams

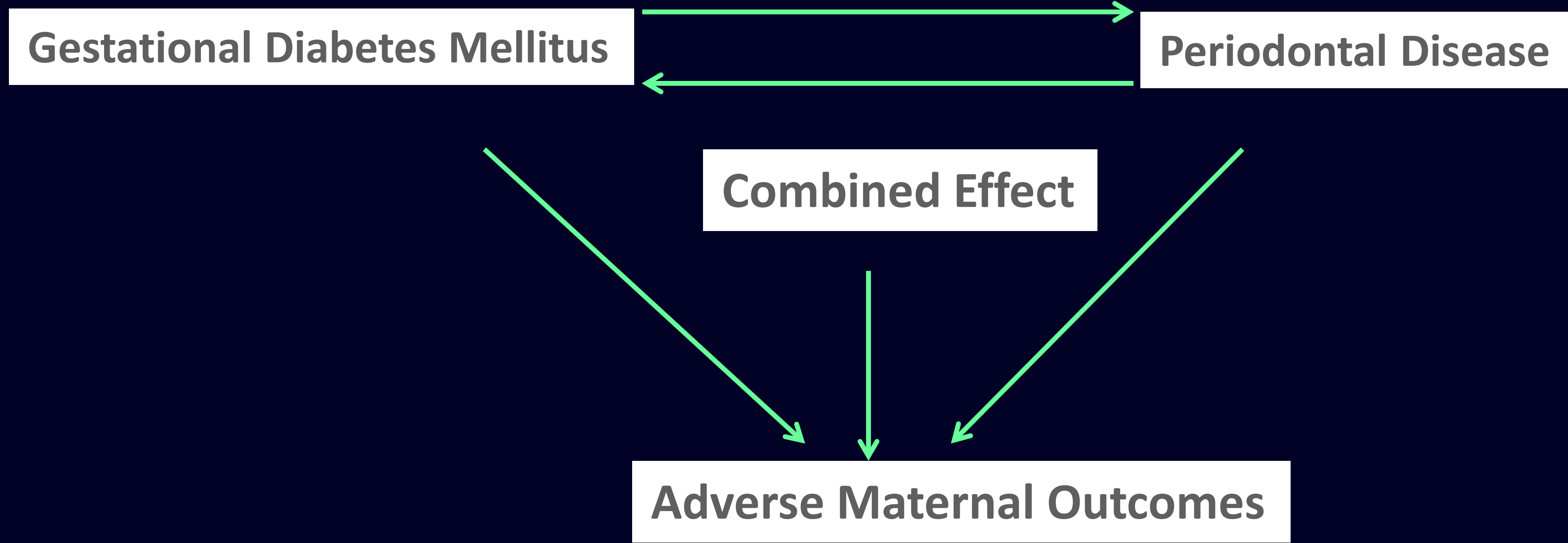
Observational Evidence: Incidence of poorer glycemic control at ~2-yrs. follow-up in Pima Indians



N for bone loss < 50% = 56
N for bone loss 50%+ =49

Source: Taylor et al., 1996

GDM-Periodontal Disease Relationship



Periodontal disease, gestational diabetes mellitus and adverse maternal outcomes

- Hypothesis: the combination of GDM and periodontal disease is associated with risk for adverse pregnancy outcome
- Study group: 153 women with GDM and 153 non-GDM pregnant controls
- Matched on age, gestational age and race/ethnicity
- Delivery-related maternal composite outcome: pre-eclampsia, premature labor, premature rupture of membranes, urinary tract infections, chorioamnionitis/funisitis, induction of labor, operative vaginal deliveries or unplanned cesarean delivery

Periodontal disease, gestational diabetes mellitus and adverse maternal outcomes, cont.

Contrasts for PD and GDM status	Odds Ratio	95% CI
PD+ GDM+ vs. PD- GDM-	2.3	1.06, 4.8
PD+ GDM+ vs. PD- GDM+	1.97	0.88, 4.4
PD+ GDM+ vs. PD+ GDM-	1.77	0.85, 3.7

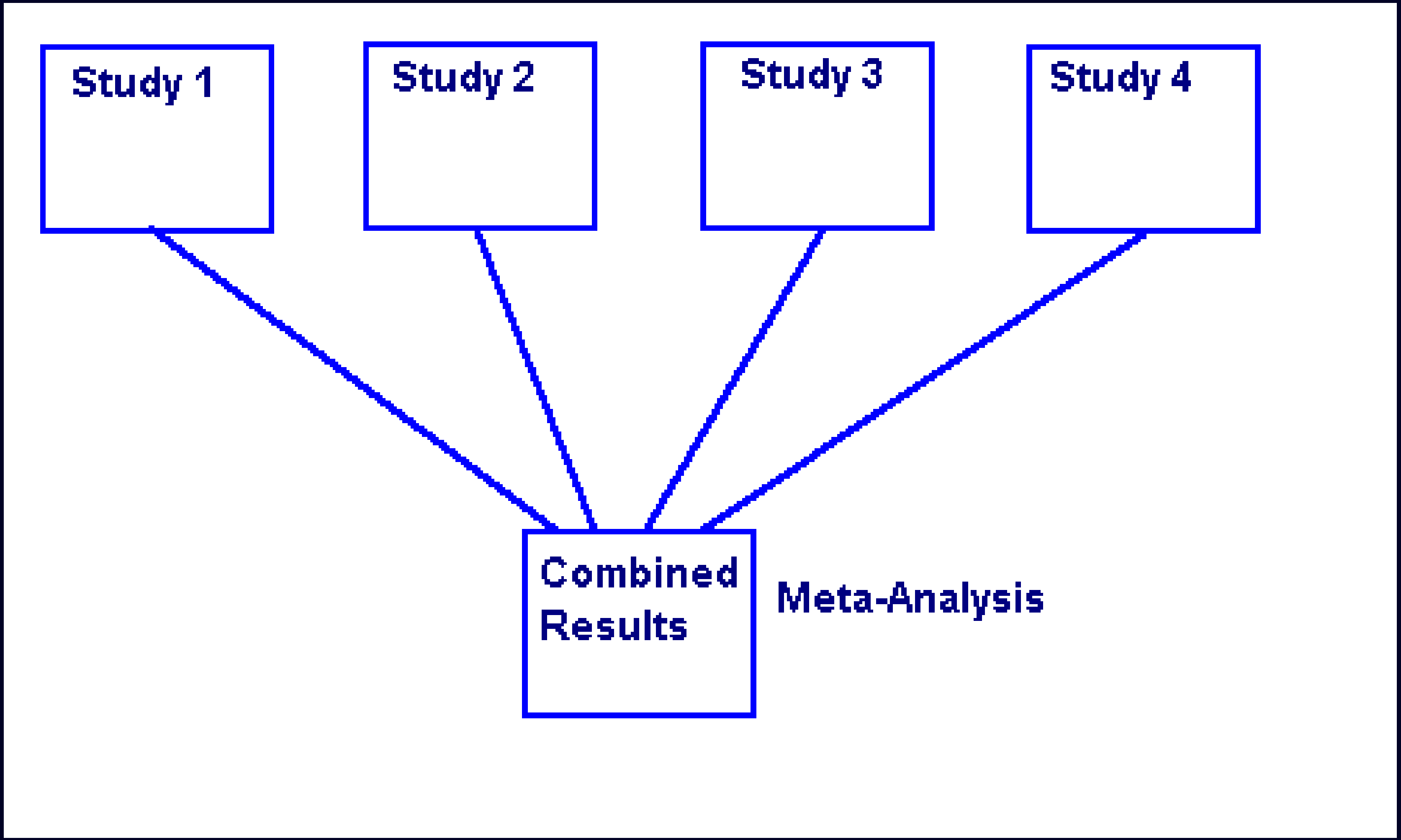
Periodontal Infection
Its Effect on Glycemic Control:

Non-surgical Periodontal Treatment Randomized Controlled Trials (RCTs)

Non-surgical periodontal therapy (routine)

Photographs courtesy of Dr. Robert Parr, UCSF)

Systematic Review & Meta-analysis



Source: SUNY- http://library.downstate.edu/EBM2/2700.htm

Meta-Analyses of Perio Intervention Studies: A1c Change

Author & Year	#	#RCT	DM Type	Pooled N	HbA1c Change	95% CI
Janket, 2005	10	1	1, 2, 1/2	456	-0.4%	-1.5, 0.7
Darre, 2008	9	9	2	485	-0.46%	-0.11, -0.82
Teeuw, 2010	5	3	2	180	-0.40%	-0.77, -0.04
Simpson, 2010 (Cochrane Rev.)	3	3	2	125	-0.40%	-0.78, -0.01
Engebretson and Kocher, 2013	9	9	2	719	-0.36%	-0.54, -0.19

Source: Adapted from Borgnakke WS . 2011

NIDCR-funded multicenter RCT (JAMA, 2013)

- **Population:** Type 2 diabetes, HbA1c 7% to < 9%, untreated chronic pdz, stable medications, N=514
- **Intervention:** Scaling and root planing, chlorhexidine rinse at baseline, SPT at 3 and 6 months
- **Control** (comparator) group: No treatment for 6 months
- **Outcome:** Difference in change in HbA1c

- **Results:**
  - Enrollment stopped early because of futility
  - Treatment group: HbA1c increased 0.17%
  - Control group: HbA1c increased 0.11%
  - No significant difference between groups: -0.05%, P=0.55

NIDCR-funded multicenter RCT (JAMA, 2013): Criticisms (J Evid Base Dent Pract, 2014)

- No significant effect of periodontal treatment would be expected because baseline A1c levels were already close to the goal for good glycemic control (A1c for enrollment was between 7% and < 9%).

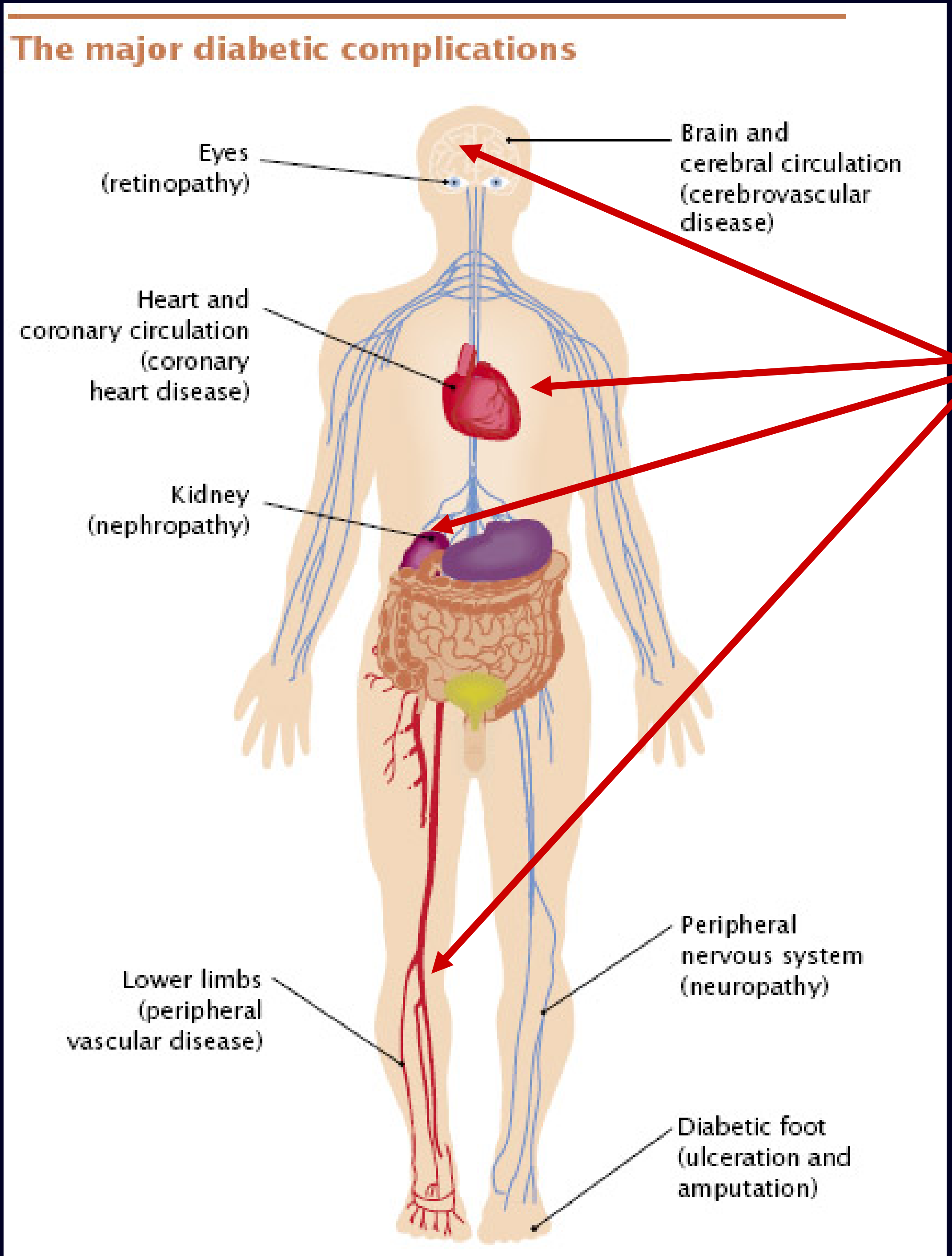
- No conclusion can be drawn regarding any effect on glycemic control because periodontal treatment failed to reach the accepted standard of care

- Pronounced obesity would mask any decrease in inflammatory response caused by successful periodontal treatment

Significance of improving of glycemic control

- Any sustained lowering of blood glucose helps delay the onset and progression of microvascular complications of diabetes
- Every percentage point reduction in HbA1c leads to a 35% reduction in the risk of microvascular complications
- Reduction of HbA1c by 0.20% is associated with a 10% reduction in mortality

Periodontal Infection and Complications of Diabetes


The major diabetic complications
Eyes
(retinopathy)
Brain and
cerebral circulation
(cerebrovascular
disease)
Heart and
coronary circulation
(coronary
heart disease)
Kidney
(nephropathy)
Peripheral
nervous system
(neuropathy)
Lower limbs
(peripheral
vascular disease)
Diabetic foot
(ulceration and
amputation)

Periodontal Disease and Complications of Diabetes

Study	N (Age)	FU #Yrs	Complication
Thorstensson 1996 Sweden	39 (36-70yrs)	6yrs	Renal & Cerebro-Cardiovascular (CVD)
Saremi 2005 USA	628 (≥35yrs)	11yrs	Cardio-renal mortality (isch. heart disease/nephropathy
Shultis 2007 USA	529 (25-79yrs)	a) 9yrs b) 15yrs	a) Macroalbuminuria b) End-stage renal disease
Li 2010 20 countries	10,958(55-88yrs)	5yrs	a) CVD mortality b) Cerebro-CVD events
Abrao 2010 Brazil	122 (28-81yrs)	Cross-sectional	Neuropathic foot ulceration
Southerland 2012 USA	6,048 (52-74yrs)	Cross-sectional	a)Carotid IMT; b)Atheroscl. plaque calcification; c)CHD
Noma 2004 Japan	73 (n/a)	Cross-sectional	Retinopathy

Source: Borgnakke, 2012

Prediabetes and Early Forms of Complications of Diabetes

Prediabetes and Early Forms of Complications of Diabetes

- Nephropathy
- Chronic kidney disease
- Small fibre neuropathy
- Diabetic retinopathy
- Increased risk of macrovascular disease

Periodontal Infection
as a Risk Factor for Developing Diabetes

Periodontal Disease and Diabetes Incidence

Study	N (Age)	FU	DM2 Outcome
Demmer 2008 USA	9,296 (50±19yrs)	17yrs	Perio extent=>DM2, 50 - 100% greater risk for diabetes
Ide 2011 Japan	5,848 (30-59yrs)	7yrs	Severe perio=>DM2; No *vs.* Severe Perio: HR=2.23
Saito 2004 Japan	961 (40-79yrs)	10yrs	Severe perio=>DM2; Dose-response: 0.13% A1c increase/mm PPD
Morita 2012 Japan	6,125 (30-69yrs)	5yrs	Sev perio=>DM2

Source: Borgnakke, 2012

Action steps/Interventions

Screening for dysglycemia in the dental care setting: Study in Michigan (Herman et. al., 2015)

- Dysglycemia: 33% of U.S. adults; 90% undiagnosed
- Dental visits: ~70%of adults visit a DDS yearly
- Question: Can screening for dysglycemia be useful in the dental care setting?
- Recent study of 1,033 patients in 13 dental practices in S.E. Michigan
- Purpose:
  - Develop and validate a tool to screen for dysglycemia
  - Assess the prevalence of previously undiagnosed prediabetes and diabetes in dental practices

Screening for dysglycemia in the dental care setting, con't.

- Population
  - Adult dental patients, ages ≥ 30 years
  - No history of diabetes
  - Visit for routine check-ups and cleanings
- Intervention/Methods
  - Questionnaire of established risk factors for dysglycemia and symptoms and signs of periodontal disease
  - Random capillary glucose
  - Routine periodontal exam as per office protocol
  - Refer to Michigan Clinical Research Unit for A1c testing
    - All with capillary glucose >=110 mg/dl or with perio. disease
    - Random sample of those with <110 mg/dl

Screening for dysglycemia in the dental care setting, con't.

- Referred to Michigan Clinical Research Unit for A1c testing
  - All with capillary glucose >=110 mg/dl or with periodontal disease (n=100/354)
  - Random sample of those with <110 mg/dl (n=81/327)

- Results from referral to MCRU (n=181)
  - Diagnosed diabetes: n=3
  - Pre diabetes: n=57
  - Normal glycemia: n=121

Screening for dysglycemia in the dental care setting, cont.

- Results: referral to MCRU (n=181)
  - Diagnosed diabetes: n=3
  - Pre diabetes: n=57
  - Normal glycemia: n=121

- Results: Estimate of prevalence of dysglycemia in the 1,033 screened participants
  - Previously undiagnosed diabetes: 13 (1.3%)
  - Previously undiagnosed prediabetes: 297 (28.7%)

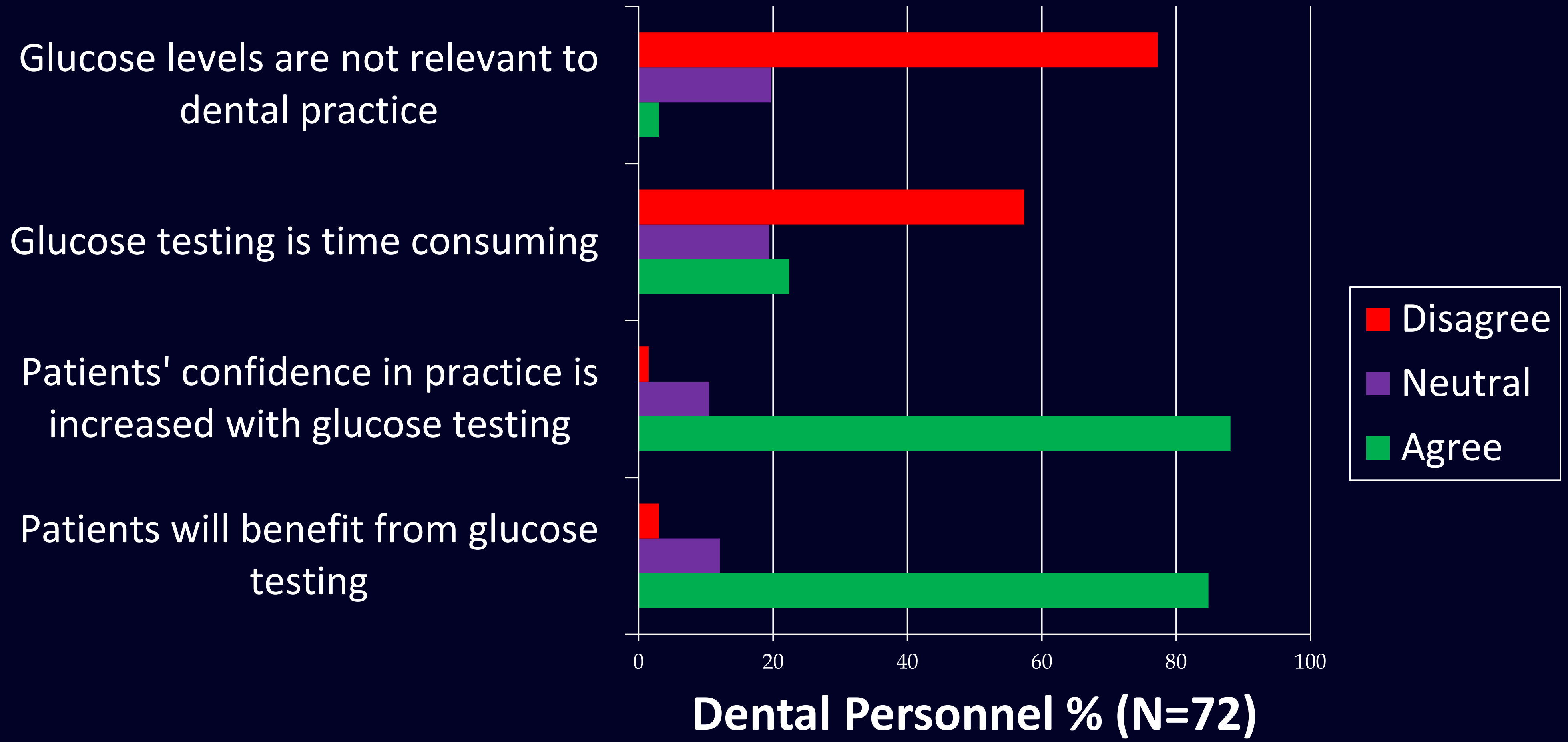
Screening for dysglycemia in the dental care setting, cont.

- Results: Performance of the screening tool
  - Adults ages 30+ years at high-risk for dysglycemia can be accurately identified using a questionnaire that assesses the following items:

    sex; history of hypertension,
    dyslipidemia history of lost teeth
    self-reported BMI

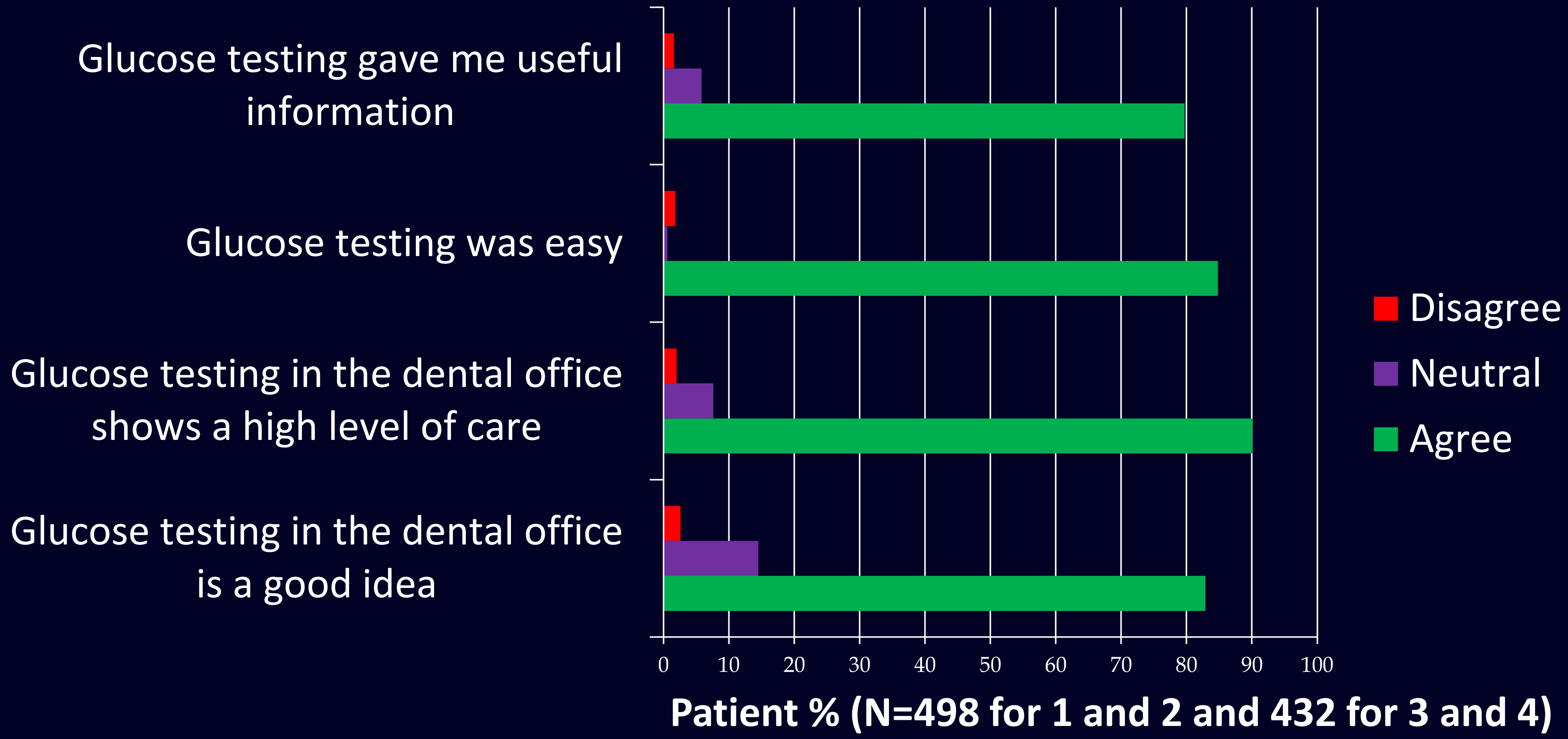
    - With random capillary glucose: Accuracy = 83%
    - Without random capillary glucose: Accuracy = 79%

Dental personnel attitudes towards blood glucose testing in 28 dental offices



Source: Barasch et.al., 2012, JADA

Patient attitudes towards blood glucose testing in the dental office



Source: Barasch et.al., 2012, JADA

Screening for dysglycemia in the dental care setting, (cont.)

- Implementation considerations/potential barriers:
  - State regulations regarding scope of practice
  - Regulatory issues : in-office laboratory testing
  - Establishing policies that support reimbursement
- Cost effective analyses
- Return on investment assessment (e.g., improving health, reducing medical costs, enhanced periodontal disease treatment and prevention

Action steps for dental care and medical care providers in addressing oral health within the context of prediabetes and diabetes

Disscussion at this time with today’s Conference participants

(if time permits)

Summary

- Reviewed cross-sectional and longitudinal evidence that supports the need to recognize the adverse effects that prediabetes as well as diabetes have on oral health
- Reviewed cross-sectional and longitudinal evidence that supports periodontal infection having adverse effects on the development of insulin resistance, prediabetes, and adverse diabetes outcomes

Summary (cont.)

- Described feasibility, potential benefits, and acceptability of screening for dysglycemia in the dental practice setting

- Discussed action steps for dental care and medical care providers to take in addressing oral health within the context of prediabetes and diabetes

Thank you for your attention

- QUESTIONS?
- Please feel free to contact me

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