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

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

**Moderate Perio:**
2+ teeth with AL $\geq 4$ mm OR 2+ teeth with PD $\geq 5$ mm at interprox. sites

**Severe Perio:**
2+ teeth with AL $\geq 6$ mm AND 1+ teeth with PD $\geq 5$ mm at interprox. sites
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

[Bar chart showing prevalence of moderate or severe periodontal disease by smoking status and diabetes status.]

- Normal
- Prediabetes
- Diabetes

Smoking status:
- Never smoker
- Former smoker
- Current smoker
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)
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 prevalent periodontitis

<table>
<thead>
<tr>
<th>Authors</th>
<th>Year</th>
<th>Location</th>
<th>GDM PD Prev</th>
<th>NO_GDM PD Prev</th>
<th>Odds Ratio</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chokwiriyachit A, et al.</td>
<td>2013</td>
<td>Thailand</td>
<td>50%</td>
<td>26%</td>
<td>3.0</td>
<td>1.2, 7.6</td>
</tr>
<tr>
<td>Xiong X, et al.</td>
<td>2009</td>
<td>U.S.</td>
<td>77%</td>
<td>57%</td>
<td>2.6</td>
<td>1.1, 6.1</td>
</tr>
<tr>
<td>Novak KF, et al.</td>
<td>2006</td>
<td>U.S.</td>
<td>9.0-31.0%</td>
<td>4.8-11.6%</td>
<td>8.0</td>
<td>P&lt;0.05</td>
</tr>
<tr>
<td>Xiong X, et al.</td>
<td>2006</td>
<td>U.S.</td>
<td>29-45%</td>
<td>14%</td>
<td>9.1</td>
<td>P&lt;0.05</td>
</tr>
<tr>
<td>Esteves L, et al.</td>
<td>2013</td>
<td>Brazil</td>
<td>40%</td>
<td>46.30%</td>
<td>0.7</td>
<td>P&gt;0.05</td>
</tr>
</tbody>
</table>
Status of the evidence for adverse effects of diabetes on periodontal health: 1967 to 2011

<table>
<thead>
<tr>
<th>Study design</th>
<th>Total # Studies +</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cohort study</td>
<td>8/9</td>
</tr>
<tr>
<td>Cross-sectional</td>
<td>93/106</td>
</tr>
<tr>
<td>Total</td>
<td>101/115</td>
</tr>
</tbody>
</table>
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

<table>
<thead>
<tr>
<th>Age Groups</th>
<th>NoDM: n=622</th>
<th>Type 2: n=225</th>
</tr>
</thead>
<tbody>
<tr>
<td>15-19</td>
<td>6</td>
<td>20</td>
</tr>
<tr>
<td>20-34</td>
<td>16</td>
<td>44</td>
</tr>
<tr>
<td>35-49</td>
<td>32</td>
<td>63</td>
</tr>
<tr>
<td>50-64</td>
<td>64</td>
<td>66</td>
</tr>
<tr>
<td>65+</td>
<td>75</td>
<td>86</td>
</tr>
</tbody>
</table>
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
Diabetes and edentulism: Pima Indians

<table>
<thead>
<tr>
<th>Age Groups</th>
<th>NoDM: n=341</th>
<th>Type 2: n=162</th>
</tr>
</thead>
<tbody>
<tr>
<td>15-19</td>
<td>25</td>
<td>27</td>
</tr>
<tr>
<td>20-34</td>
<td>19</td>
<td>18</td>
</tr>
<tr>
<td>35-49</td>
<td>8</td>
<td>14</td>
</tr>
<tr>
<td>50-64</td>
<td>14</td>
<td>36</td>
</tr>
<tr>
<td>65+</td>
<td>0</td>
<td>60</td>
</tr>
</tbody>
</table>
Diabetes, prediabetes and root caries
Root fragments

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
Proinflammatory state
Chronic over-expression of cytokines
Insulin resistance

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

II-1β
II-6
TNFα

Chronic inflammation
Visceral obesity
Proinflammatory state
Chronic over-expression of cytokines
Insulin resistance

Pancreatic beta cell damage
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

<table>
<thead>
<tr>
<th>Study</th>
<th>N (Age)</th>
<th>#Years FU</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demmer 2010 Germany</td>
<td>2,793 (20-81yr)</td>
<td>5yrs</td>
<td>HbA1c increase</td>
</tr>
<tr>
<td>Saito 2004 Japan</td>
<td>961 (40-79yr)</td>
<td>10yrs</td>
<td>HbA1c increase, Glucose intolerance</td>
</tr>
</tbody>
</table>
Periodontal Infection
Effect on Glycemic Control:
Observational Epidemiological Studies
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

Source: Taylor et al., 1996
GDM-Periodontal Disease Relationship

Gestational Diabetes Mellitus → Combined Effect → Adverse Maternal Outcomes

Periodontal Disease → Combined Effect → Adverse Maternal Outcomes
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.

<table>
<thead>
<tr>
<th>Contrasts for PD and GDM status</th>
<th>Odds Ratio</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>PD+ GDM+ vs. PD- GDM-</td>
<td>2.3</td>
<td>1.06, 4.8</td>
</tr>
<tr>
<td>PD+ GDM+ vs. PD- GDM+</td>
<td>1.97</td>
<td>0.88, 4.4</td>
</tr>
<tr>
<td>PD+ GDM+ vs. PD+ GDM-</td>
<td>1.77</td>
<td>0.85, 3.7</td>
</tr>
</tbody>
</table>
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

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

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

- 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)
- Lower limbs (peripheral vascular disease)
- Peripheral nervous system (neuropathy)
- Diabetic foot (ulceration and amputation)
## Periodontal Disease and Complications of Diabetes

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

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

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

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 $\geq 110$ 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

Glucose testing gave me useful information
Glucose testing was easy
Glucose testing in the dental office shows a high level of care
Glucose testing in the dental office is a good idea

Patient % (N=498 for 1 and 2 and 432 for 3 and 4)

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

Discussion 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

George.Taylor@ucsf.edu

University of California San Francisco School of Dentistry