The SEARCH for Diabetes in Youth Study

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Outline of Presentation

- Scientific rationale
- SEARCH study design
- SEARCH contributions:
  - Burden of diabetes in youth
  - Defining diabetes type
  - Characteristics of youth with diabetes
  - Quality of care
  - Risk factors for chronic complications
- Plans for the future
- Informing Interventions
Scientific Rationale

• Increase in T2D in youth in several populations – especially minority
• Increase in T1D incidence reported worldwide – limited US data
• Reports of “atypical” diabetes with mixed phenotypes in youth
SEARCH Design

De-duplication & validation

Local Site Registry

SEARCH Cohort
- Physical exam
- Blood draw & storage
- Urine collection
- Questionnaires

Follow up

SEARCH Registry

Data Collection

De-identify
POPULATIONS UNDER SURVEILLANCE
## Denominator:
### Youth Under Surveillance

<table>
<thead>
<tr>
<th>Center</th>
<th>Annual #</th>
</tr>
</thead>
<tbody>
<tr>
<td>California (health plan site)</td>
<td>792,188</td>
</tr>
<tr>
<td>Colorado</td>
<td>1,405,205</td>
</tr>
<tr>
<td>Native American Sites</td>
<td>91,542</td>
</tr>
<tr>
<td>Ohio</td>
<td>558,911</td>
</tr>
<tr>
<td>South Carolina</td>
<td>1,182,077</td>
</tr>
<tr>
<td>Washington</td>
<td>966,045</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>4,995,968</strong></td>
</tr>
</tbody>
</table>
## Networks of Providers and Facilities

<table>
<thead>
<tr>
<th>Clinical Site</th>
<th>Pediatric Endocrinologists</th>
<th>Other Case Sources</th>
</tr>
</thead>
<tbody>
<tr>
<td>California</td>
<td>9 Pediatric Endocrinologists</td>
<td>Kaiser Permanente Southern California clinical and administrative data systems (electronic health records)</td>
</tr>
</tbody>
</table>
| Colorado         | 2 Pediatric Endocrinology practices                              | Hospitals (8)  
Other (pediatricians, adult endocrinologists, CDEs) (~10)  
Community Health Centers (4)  
Navajo Nation: 8 Indian Health Service units |
| Ohio             | Pediatric Endocrinology practice in Cincinnati  
Children’s Hosp (92%)                                           | Hospitals (15)  
Other (adult endocrinologists, CDEs) (~10)  
Third-party payers (5)  
Cincinnati Health Dept |
| South Carolina   | 6 Pediatric Endocrinology practices                              | Hospitals (6)  
Other (adult endocrinologists, FQHC, other) (~10) |
| Washington       | 3 Pediatric Endocrinology practices                              | Hospitals (9)  
Other (adult endocrinologists, community clinics, CDEs) (~10) |

FQHC = Federally qualified health center; CDE = certified diabetes educator
Numerator: Eligibility

- Persons with physician diagnosed diabetes
- Aged less than 20 in 2001 and 2009 (prevalence) or age less than 20 at diagnosis in 2002 onwards (incidence)
- Residents of the population defined or members of health plans or users of the IHS
- Not active duty military, not institutionalized
- Not gestational diabetes mellitus (GDM) only
SEARCH CONTRIBUTION

Burden of Diabetes in Youth
Incidence of Type 1 Diabetes in 2002-2003, by Age and Race/Ethnicity

SEARCH Study Group, JAMA 297(24), 2716, 2007
Incidence of Type 2 Diabetes in 2002 -2003, by Age and Race/Ethnicity
Trends in T1D Prevalence, 2001-2009, by Sex, Age and Race/Ethnicity

Dabelea & Mayer-Davis et al., JAMA, 2014

* Statistically significant difference in prevalence between 2001 and 2009
Trends in T2D Prevalence, 2001-2009, by Sex and Age and Race/Ethnicity

Dabelea & Mayer-Davis et al., JAMA, 2014
Burden of Diabetes in US Youth

• Applied to US Census data, SEARCH estimated:
  • 191,986 youth in the US had physician-diagnosed diabetes in 2009
  • 166,984 with T1D; 20,262 with T2D; 4,740 with ‘other’ types
  • ~18,400 youth are diagnosed with T1D each year
  • ~5,100 youth are diagnosed with T2D each year

Projected Number (bars) and Prevalence (line) of T1D and T2D in People aged <20 Years

SEARCH CONTRIBUTION
DEFINING DIABETES TYPE

With increasing obesity, youth with T1D may be overweight or obese, causing confusion about the correct diagnosis.
Classification of Diabetes Type based on Autoimmunity and Insulin Sensitivity

- **Autoimmunity**
  - **DA +**
    - **Insulin Sensitivity**
      - **Sensitive** (IS ≥ 8.15)
      - **Resistant** (IS < 8.15)
  - **DA -**
    - **Insulin Sensitivity**
      - **Sensitive** (IS ≥ 8.15)
      - **Resistant** (IS < 8.15)

**DA+** Positive for IA2 or GAD65 autoantibody (measured using NIDDK standardized assay)

* Insulin Sensitivity = \( \exp [4.64725 - 0.02032 \times (\text{waist, cm}) - 0.09779 \times (\text{HbA1c, %}) - 0.00235 \times (\text{TG, mg/dl})] \);

Resistant = IS index below the 25th percentile for NHANES youth (IS < 8.15)
Sensitive = IS index > the 25th percentile for NHANES youth (IS > 8.15)

Classification of Diabetes Type based on Autoimmunity and Insulin Sensitivity (cont.)

- Autoimmune +IS (54.5%) or non-autoimmune +IR (15.9%) categories align with traditional descriptions of T1D or T2D.
- The autoimmune + IR group (19.5%) likely represents individuals with T1D autoimmune diabetes and obesity.
- The non-autoimmune + IS group (10.1%) represents an etiologically mixed category & requires further testing.
- For the purpose of public health surveillance, the provider-assignment of diabetes type agrees well with the etiological assessment.

Dabelea, et al. *Diabetes Care* : 34; 1628; 2011
Algorithm for Classification of Pediatric Diabetes

1. **Diabetes**
   - **Autoantibodies present** (GADA, IA-2A, ZnT8, IAA, etc.)
   - **No Autoantibodies**
     - **Insulin Sensitive (Normal waist)**
       - **Additional Testing**
         - **Type 1 Diabetes**
         - **MODY**
         - **Secondary Diabetes**
         - **Type 2 Diabetes**
         - **Other Genetic**
     - **Insulin Resistant (Large waist)**
SEARCH CONTRIBUTION

Characteristics of Youth with Diabetes
Prevalence of Socioeconomic Indicators

Type 1

- Household Income <$25K
- Highest Parental Ed. <HS

Type 2

- Household Income <$25K
- Highest Parental Ed. <HS

Diabetes Care (Suppl 2), 2009
Prevalence of Overweight and Obesity

Type 1

Type 2

NHW  AA  H  API  AI

Overweight
Obese

Overweight
Obese

Diabetes Care (Suppl 2), 2009
Prevalence of Selected Health Behaviors

Type 1

Type 2

Diabetes Care (Suppl 2), 2009
SEARCH CONTRIBUTION

Quality of Care
Prevalence of Poor Glycemic Control (A1c ≥ 9.0%)

<table>
<thead>
<tr>
<th>Race/Ethnicity</th>
<th>Type 1 (%)</th>
<th>Type 2 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-Hispanic White</td>
<td>12.3</td>
<td>12.2</td>
</tr>
<tr>
<td>African American</td>
<td>35.5</td>
<td>22.3</td>
</tr>
<tr>
<td>Hispanic</td>
<td>27.3</td>
<td>27.4</td>
</tr>
<tr>
<td>Asian/Pacific Islander</td>
<td>26.0</td>
<td>36.4</td>
</tr>
<tr>
<td>Native American</td>
<td>52.2</td>
<td>43.8</td>
</tr>
</tbody>
</table>

Percentage of Youth Reporting Receipt of Test/Measurement

- A1c Testing: 74.2%
- Lipid Profile: 86.7%
- BP Measurement: 93.0%
- Microalbuminuria Measured: 81.6%
- Eye Exam: 62.9%

SEARCH CONTRIBUTION

Risk of Chronic Complications
Prevalence of Cardiovascular Risk Factors, by Race/Ethnicity

Rodriguez B, Diabetes Care 2006;
Prevalence of Elevated Albumin: Creatinine Ratio (ACR) by Diabetes Type

Maahs et al., *Diabetes Care* 2007
Prevalence of Other Microvascular Complications* by Diabetes Type: Pilot Study

*Retinopathy: any evidence in either eye
Neuropathy: Michigan Neuropathy Screening Instrument score >2

Mayer-Davis et al., *Diabetic Med.* 2012; 29:1148-1152
Jaiswal M et al., *Diabetes Care* 2013 36:3903 – 3908
SEARCH-Navajo Study:
Example of American Indian participation in SEARCH
Who is Eligible for SEARCH-Navajo?

• Patients with **physician diagnosed** diabetes (NOT GDM)
  • Age less than 20 on December 31 of the year of diagnosis (incidence) or age < 20 on December 31 of prevalent year (2001, 2009)

• **Active users of the Indian Health System**
  (users in the past 3 years)

• Not active duty military, not institutionalized in prevalent year / at diagnosis
## SEARCH-Navajo Case Ascertainment

<table>
<thead>
<tr>
<th>Service Unit</th>
<th>Denominator</th>
<th>RPMS Prevalent 2001 Incident 2002 Cases</th>
<th>Valid/Registered Prevalent and 2002 Incident Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crownpoint</td>
<td>8,351</td>
<td>12</td>
<td>11</td>
</tr>
<tr>
<td>Chinle</td>
<td>15,552</td>
<td>28</td>
<td>11</td>
</tr>
<tr>
<td>Ft. Defiance</td>
<td>10,987</td>
<td>32</td>
<td>15</td>
</tr>
<tr>
<td>Gallup</td>
<td>17,683</td>
<td>44</td>
<td>15</td>
</tr>
<tr>
<td>Kayenta</td>
<td>8,202</td>
<td>45</td>
<td>10</td>
</tr>
<tr>
<td>Shiprock</td>
<td>21,098</td>
<td>50</td>
<td>30</td>
</tr>
<tr>
<td>Tuba City</td>
<td>9,871</td>
<td>20</td>
<td>11</td>
</tr>
<tr>
<td>Winslow</td>
<td>6,272</td>
<td>12</td>
<td>9</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>98,016</strong></td>
<td><strong>233</strong></td>
<td><strong>112</strong></td>
</tr>
</tbody>
</table>
Prevalence of DM in 2001 (per 1,000) among Navajo Youth

Dabelea et al. *Diabetes Care* 2009
Prevalence of DM in Other American Indian/Alaska Native Youth

• AI/AN youth, based on RPMS data, no medical record validation (Acton K, Am J Pub Health 92; 2002)
  • <15 years: 1.2/1,000
  • 15-19 years: 5.4/1,000
Incidence of DM in 2002-2004 (per 100,000/year), among Navajo Youth

Dabelea et al. Diabetes Care 2009
### Characteristics of Navajo Youth with Diabetes, By Diabetes Type

<table>
<thead>
<tr>
<th></th>
<th>Type 1</th>
<th>Type 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at visit (years): mean (range)</td>
<td>15.3 (7-20)</td>
<td>17.4 (11.8-21.6)</td>
</tr>
<tr>
<td>Duration of Diabetes (years): mean (range)</td>
<td>6.2 (0.3-15.8)</td>
<td>3.6 (0.1-8)</td>
</tr>
<tr>
<td>FCP (ng/ml): mean (range)</td>
<td>0.7 (0.2-3.5)</td>
<td>3.7 (0.2-11.4)</td>
</tr>
<tr>
<td>% High CESD scores (≥ 24)</td>
<td>14.3%</td>
<td>21.9%</td>
</tr>
<tr>
<td>% High waist (≥ 90th percentile)</td>
<td>33%</td>
<td>81%</td>
</tr>
<tr>
<td>% BMI ≥ 95th percentile</td>
<td>26.7%</td>
<td>67.2%</td>
</tr>
<tr>
<td>% High blood pressure</td>
<td>13.3%</td>
<td>58.6%</td>
</tr>
<tr>
<td>% Microalbuminuria</td>
<td>6.7%</td>
<td>25.8%</td>
</tr>
<tr>
<td>% Poor glycemic control (HbA1c≥9.5%)</td>
<td>53%</td>
<td>41%</td>
</tr>
<tr>
<td>% High Triglycerides (≥110 mg/dl)</td>
<td>53%</td>
<td>72%</td>
</tr>
<tr>
<td>% Low HDLc (≤ 40 mg/dl)</td>
<td>27%</td>
<td>40%</td>
</tr>
</tbody>
</table>
Treatment Patterns of Navajo Youth with Type 1 and Type 2 Diabetes

<table>
<thead>
<tr>
<th></th>
<th>Type 1</th>
<th>Type 2</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>DM Treatment (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insulin 1-2 inj/day</td>
<td>33.3%</td>
<td>20.7%</td>
</tr>
<tr>
<td>Insulin 3+ inj/day</td>
<td>66.6%</td>
<td>6.8%</td>
</tr>
<tr>
<td>Oral agents only</td>
<td>0%</td>
<td>72.5%</td>
</tr>
<tr>
<td><strong>On Metformin (%)</strong></td>
<td>6.6%</td>
<td>68.9%</td>
</tr>
<tr>
<td><strong>Lipid Lowering Treatment (%)</strong></td>
<td>0%</td>
<td>5.2%</td>
</tr>
<tr>
<td><strong>HTN Treatment (%)</strong></td>
<td>0%</td>
<td>25.8%</td>
</tr>
</tbody>
</table>
PLANS FOR THE FUTURE

SEARCH 4
Registry Study

- **Continue to conduct sentinel surveillance of diabetes:**
  - SEARCH Registry study can be utilized to provide national estimates of prevalence, incidence, presentation, temporal trends, mortality, without the need for a national system
  - Can SEARCH be expanded to include other AI tribes/IHS participation?

- **Major Research questions:**
  - Will the incidence of T1D continue to rise or will there be a leveling off, as recently reported in Scandinavian countries?
  - Will the incidence of T2D rise, or will there be a leveling off, particularly in the highest risk groups (e.g., AI)?
Cohort Study

• **Continue the longitudinal follow up** of SEARCH inception cohort of young adults with T1D and T2D

• **Major Research Questions:**
  • What is the clinical evolution of acute and chronic early complications of diabetes among youth and young adults with T1D or T2D diagnosed in childhood?
  • What are the drivers of early complications of diabetes diagnosed in childhood, and do these drivers differ for T1D and T2D?
INFORMING INTERVENTIONS
Reducing Risk for Type 2 Diabetes in American Indian Youth

Partnership: UNC Chapel Hill (Beth Mayer-Davis), UC Denver (Dana Dabelea), East Band Cherokee and Navajo Nation
A compelling need in AI communities

• High risk for development of T2D
• SEARCH for Diabetes in Youth Study
  • AI youth had highest T2D incidence and prevalence
• Higher overweight prevalence in AI schoolchildren than other subgroups
• Majority of AI adults in west and southwest affected by overweight/obesity
Previous Efforts

• Strong data from efforts to prevent T2D in adults with lifestyle modification
  • Diabetes Prevention Program
    • Key mediators: weight loss, lower percent calories from fat, increased physical activity
  • Native Lifestyle Balance (NLB) Program
    • Applied to AI group-based community settings
• Data from youth interventions is limited, with mixed results
  • The HEALTHY Study, The Pathways Project
• Success in multi-component programs that provide physical activity and support for dietary change, while involving families and key community partners
Overarching Goal...

...to develop, deliver and rigorously evaluate a novel three-component intervention designed to reduce risk factors for T2D in Cherokee and Navajo AI youth.

The intervention is designed for eventual broad, sustainable dissemination for AI and other high-risk communities.
Research Aims

• Aim 1 – to further develop the TTP intervention through Community-Based Participatory Research process

• Aim 2 – To implement to TTP intervention in an 8-month pilot and feasibility trial in Cherokee, NC and Shiprock, NM
Intervention Development
3 Components

Active Learning: 10 classes
- Hands-on activities
- Physical activity
- Goal tracking

Toolbox materials
- Resources to be used as-needed by staff, based on needs of participating families
- Follows Social Ecological Model

Motivational Interviewing (MI)
- Person-centered counseling technique
- Used to strengthen an individual’s motivation and commitment for change by eliciting that individual’s own arguments for change (problem solving skills)
Intervention Development

• Basis for physical activity
  • At least 60 min. per day
  • Fitness-focused, age-appropriate suitable for overweight or obese, unfit children
  • Culturally relevant

• Basis for diet & weight loss
  • Traffic Light Guide
  • 5-2-1-0 campaign
    • 5 F&V
    • <2 hr screen time
    • 1 hr physical activity
    • 0 SSBs
Intervention Development

August 2014 –
Baseline measurements, randomization

January 2015 to April –
2 booster classes, 2 booster MI sessions

September to December –
10 AL classes, 3 MI sessions, Toolbox as needed

May 2015 –
End-of-study measurements
Aim 2: Implementing pilot study

• August 2014 – May 2015
• 2 sites – Cherokee, NC and Shiprock, NM
• 30 youth enrolled at each site
  • (15 control/15 intervention)
Pilot Study - Outcomes

• Primary outcomes
  • Change in BMI
  • Change in fasting insulin

• Secondary outcomes
  • Change in HbA1c
  • Change in fasting glucose

• Other measures
  • Intervention acceptability
  • Changes in diet/physical activity behaviors
Thank You

The SEARCH for Diabetes in Youth Study is indebted to the many youth and their families, and their health care providers, whose participation made this study possible.