Diabetes Management in Toddlers/Preschoolers (<6 yo)

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T1D Exchange (T1DX) Registry and the Prospective Diabetes Follow-up Registry (DPV)

- T1DX: ~26,000 participants with Type 1 Diabetes (T1D) from 70 diabetes clinics across the U.S.
  - Data obtained from both medical chart review and participant questionnaires

- DPV: includes 85,439 patients with all types of diabetes from both Austria and Germany
  - Data documented locally by participating centers in electronic health record. Twice yearly, data exported for central analyses

Maahs, D et al, Diabetologia 57: 1578, 2014
### Insulin Pump vs. MDI in Children <6yo in the T1D Registry
(Blackman, SM, Chase, HP et al, Pediatric Diabetes, pre-press, 2014)

#### T1DX

- 669 children from 52 U.S. clinics <6yo and T1D>1yr
- 50% treated with CSII (337) or MDI (332)
- CSII group: ↑parent education and income (P<0.006)

<table>
<thead>
<tr>
<th></th>
<th>CSII</th>
<th>MDI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age</td>
<td>4.9yr</td>
<td>4.9 yr</td>
</tr>
<tr>
<td>Mean T1D duration</td>
<td>2yr</td>
<td>1 yr</td>
</tr>
<tr>
<td>SMBG/Day</td>
<td>8</td>
<td>6</td>
</tr>
<tr>
<td>Mean HbA1c</td>
<td>7.9</td>
<td>8.5 (P=0.001, Adjusted)</td>
</tr>
<tr>
<td>Severe Hypoglycemia</td>
<td>12%</td>
<td>8% (P=0.20)</td>
</tr>
<tr>
<td>DKA in past 12 mo</td>
<td>10%</td>
<td>8% (P=0.58)</td>
</tr>
<tr>
<td>CGM use</td>
<td>12%</td>
<td>2.9% (P=0.001)</td>
</tr>
</tbody>
</table>
Methods: Compare T1DX with GER/AUS Preschoolers

- 2,622 young children < 6 years of age, with T1D duration ≥1 year
  - 674 participants from the T1DX
  - 1,948 patients from both Germ/Aus

- Median HbA1c over the past year, excluding any values obtained within 3 months of diagnosis, was used to represent HbA1c

Maahs, D et al, Diabetologia 57: 1578, 2014
## Participant Characteristics by Registry

<table>
<thead>
<tr>
<th>Metric</th>
<th>T1DX (n=674)</th>
<th>GER/AUS (n=1948)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>4.9 (4.0, 5.5)</td>
<td>5.0 (4.1, 5.5)</td>
<td>0.32</td>
</tr>
<tr>
<td>Sex, % male</td>
<td>58%</td>
<td>53%</td>
<td>0.03</td>
</tr>
<tr>
<td>T1D duration, years</td>
<td>2.0 (1.0, 3.0)</td>
<td>1.8 (1.3, 2.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BMI Z score</td>
<td>0.85 (0.30, 1.50)</td>
<td>0.84 (0.26, 1.44)</td>
<td>0.33</td>
</tr>
<tr>
<td>Pump Use, %</td>
<td>50%</td>
<td>74%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total daily insulin, units/kg/d</td>
<td>0.68 (0.56, 0.83)</td>
<td>0.66 (0.54, 0.80)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>% prandial insulin</td>
<td>62% (50%, 71%)</td>
<td>66% (55%, 74%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SMBG/day</td>
<td>7.0 (5.0, 9.0)</td>
<td>8.0 (6.0, 10.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CGM use, %</td>
<td>7%</td>
<td>7%</td>
<td>0.40</td>
</tr>
</tbody>
</table>
Pump vs. Injection Users

Number of Boluses/Short-acting Injections per Day

- **Pump Users**
  - U.S.: 6.0
  - Germany/Austria: 6.0

- **Injection Users**
  - U.S.: 3.0
  - Germany/Austria: 3.0

*P < 0.001 for both comparisons*
Median HbA1c (%)

- **All Pump Users**: 8.2% for T1DX, 7.4% for GER/AUS
- **Pump Users**: 7.9% for T1DX, 7.4% for GER/AUS
- **Injection Users**: 8.5% for T1DX, 7.4% for GER/AUS

Significance Levels:
- **P<0.001** for all groups.
Percent with HbA1c <8.5%

- All Pump Users: 66%
- Injection Users: 54%
- Pump Users: 79%
- Injection Users: 88%

P<0.001 for all
Percent with HbA1c < 7.5%

- **All**: 22% (T1DX) vs. 56% (GER/AUS), P < 0.001 for all
- **Pump Users**: 22% (T1DX) vs. 30% (GER/AUS)
- **Injection Users**: 14% (T1DX) vs. 58% (GER/AUS)
HbA1c

ADA rational for HbA1c <8.5% in 0-6 yo’s:*

- Vulnerability to hypoglycemia
- Insulin sensitivity
- Unpredictability in dietary intake and physical activity

The ADA also notes:
- Goals should be individualized and lower goals may be reasonable based on benefit-risk assessment.
- A lower goal (<8.0%) is reasonable if it can be achieved without excessive hypoglycemia

* Clinical Practice Recommendations, 37,S51,Jan,2014
New ADA Goal: All children with type 1 diabetes should aim for an HbA1c level <7.5%

ISPAD (Int’l Society for Pediatric and Adolescent Diabetes) has recommended <7.5% for all children for many years.

The consequences of the new recommendations are unknown

Comparing the two groups may provide insight in relation to the safety of the new ADA recommendations
Percent with ≥1 SH Event in Past Year

<table>
<thead>
<tr>
<th>Category</th>
<th>All</th>
<th>Pump Users</th>
<th>Injection Users</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1DX</td>
<td>3%</td>
<td>3%</td>
<td>3%</td>
</tr>
<tr>
<td>GER/AUS</td>
<td>2%</td>
<td>2%</td>
<td>3%</td>
</tr>
<tr>
<td>Significance</td>
<td>P=0.19</td>
<td>P=0.22</td>
<td>P=0.72</td>
</tr>
</tbody>
</table>
Percent with \( \geq 1 \) SH Event in Past Year by HbA1c

<table>
<thead>
<tr>
<th>HbA1c Group</th>
<th>T1DX</th>
<th>GER/AUS</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;7.5%</td>
<td>3.0%</td>
<td>1.6%</td>
</tr>
<tr>
<td>7.5-&lt;8.5%</td>
<td>2.6%</td>
<td>2.3%</td>
</tr>
<tr>
<td>( \geq 8.5% )</td>
<td>2.9%</td>
<td>2.6%</td>
</tr>
</tbody>
</table>

P=0.97

P=0.46
Physiology: Decreased Epinephrine Responses in Children with T1D

(DirecNet, Diabetes Care, 32:1954, 2009)

Subjects:
- 14 children 4-7 yo; duration 3.3 years
- 14 adolescents 12-17 yo; duration 6.6 years

No epinephrine response (>3SD above baseline) to insulin-induced hypoglycemia (<60 mg/dL [<3.3 mmol/L])
- 9 of 14 young children (average 47 → 82 pg/mL)
- 8 of 14 adolescents (average 27 → 71 pg/mL)

14 non-diabetic adolescents increased from 77 to 582 pg/mL in response to hypoglycemia

Glucagon levels did not increase with hypoglycemia in young children or adolescent subjects with T1D
Later Sequellae of Early-Onset T1D*

- **Early-Age Diagnosis of T1D:**
  Several studies have documented worse outcomes across a variety of cognitive domains, including: IQ, executive function, learning and memory, and processing speed.

- **Severe Hypoglycemia** (Seizure or loss of consciousness)
  Many (at least 15) studies have noted poorer cognitive outcomes.

- **Chronic Hyperglycemia (+DKA)**
  Fewer studies available, but associated with abnormal grey and white matter volumes, decreased processing speed and reduced verbal intelligence.

Cameron F, et al, Diabetes Care 37,1554,2014: Neurologic changes from DKA at new-onset T1D.
Percent with ≥1 DKA Event in Past Year

- **All**: 6% (P < 0.001)
- **Pump Users**: 3% (P = 0.02)
- **Injection Users**: 1% (P < 0.001)
Percent with ≥1 DKA Event in Past Year by HbA1c

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<th>HbA1c Group</th>
<th>T1DX</th>
<th>GER/AUS</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;7.5%</td>
<td>0.8%</td>
<td>2.3%</td>
</tr>
<tr>
<td>7.5-%&lt;8.5%</td>
<td>4.1%</td>
<td>3.0%</td>
</tr>
<tr>
<td>≥8.5%</td>
<td>11.0%</td>
<td>6.8%</td>
</tr>
</tbody>
</table>

P<0.001, P=0.004
The data from Germany and Austria indicate that HbA1c levels of <7.5% can be frequently achieved in children with T1D <6 years old.

Improved metabolic control of T1D in young patients decreases the risk of DKA without increasing the risk of SH.

Sub-optimal control in young patients in the T1DX may relate to less frequent use of insulin pumps, SMBG and insulin boluses and the higher HbA1c targets in this age group that were recommended in the U.S.

“Time will tell.”
Questions? “Practical Ways to Achieve Targets in Diabetes Care:”
### Basal Insulin Use
#### Lantus vs. NPH
(Dixon, Chase HP et al, Ped Diab, 6:150-154, 2005)

128 Preschoolers (<6yo): 64 began glargine insulin

<table>
<thead>
<tr>
<th></th>
<th>Pre-study – 6 mo.</th>
<th>Study - 6 mo.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total SH</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>A. Lantus</strong></td>
<td>14</td>
<td>3</td>
</tr>
<tr>
<td><strong>B. NPH</strong></td>
<td>7</td>
<td>6</td>
</tr>
<tr>
<td><strong>Nighttime SH</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>A. Lantus</strong></td>
<td>12</td>
<td>1</td>
</tr>
<tr>
<td><strong>B. NPH</strong></td>
<td>1</td>
<td>3</td>
</tr>
</tbody>
</table>