Diabetes And Technology:

The Time Is Now!
Research Updates And Upcoming Great Tools For Diabetes

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Diabetes and Technology Today

- Four CGM systems approved in the last 12 months!
- Non-adjunctive use of CGM trend arrows approach
  - The Endocrine Society Approach
- Hybrid-closed loop system approval
  - Northwestern Experience
- Medicare approval of DEXCOM G5 and FreeStyle Flash Libre
- What is next??!!! More CGM, more hybrid closed loop, more technology!!!
Average Current A1c by Age

*≤2 years old and ≥80 years old are pooled.
CGM Users Have Lower HbA1c!

- **<13 years**
  - Injection only: 8.8%
  - Injection + CGM: 7.8%
  - Pump only: 8.5%
  - Pump + CGM: 7.8%
  - N=3571

- **13-<26 years**
  - Injection only: 9.5%
  - Injection + CGM: 8.3%
  - Pump only: 8.9%
  - Pump + CGM: 8.7%
  - N=8269

- **≥26 years**
  - Injection only: 7.4%
  - Injection + CGM: 7.4%
  - Pump only: 8.1%
  - Pump + CGM: 7.8%
  - N=5185
Benefits Of CGM Therapy

- Improve overall glycemic control
- Reduce hypoglycemia/hyperglycemia and glycemic variability
- Enhance patient / family confidence in diabetes self-care or family management
- Reduce worries related to fear of hypoglycemia and / or hyperglycemia
This Is Where It All Started!
The REPLACE-BG Study
Clinical Evidence Demonstrating Safety and Non-Inferiority of Therapeutic CGM vs. SMBG
Background

- Prior to December 2016, commercially available CGM systems in the US were FDA-approved only as adjunctive devices to information obtained from standard home blood glucose meters.

- Even when the FDA labeling limited CGM use to an adjunct-only tool, many CGM users were making insulin dosing decisions by CGM alone.
REPLACE-BG Study

- **Objective**: To determine whether the routine use of CGM without BGM confirmation is as safe and effective as CGM used as an adjunct to BGM

- 226 participants randomly assigned 2:1 to either CGM-only or CGM+BGM group
  - Both groups used Dexcom™ G4 Platinum CGM System® with an enhanced algorithm (software 505) and Contour Next BGM

- **Primary Outcome**: Time in range 70-180 mg/dl, measured with CGM over the full 6 months of the study

Primary Outcome: Mean time 70-180 mg/dL

Hypoglycemia

Hyperglycemia

Hyperglycemia rates at 26 weeks compared to baseline:

- **>180 mg/dL**
  - Baseline: 33%
  - CGM Only: 35%
  - CGM + BGM: 31%
  - P-value: 0.88

- **>250 mg/dL**
  - Baseline: 8%
  - CGM Only: 9%
  - CGM + BGM: 7%
  - P-value: 0.65

- **>300 mg/dL**
  - Baseline: 2%
  - CGM Only: 2%
  - CGM + BGM: 2%
  - P-value: 0.72

Use of CGM without confirmatory BGM measurements is as safe and effective as using CGM adjunctively to BGM testing in well-controlled adults with T1D at low risk for severe hypoglycemia.
Need Trend Arrow AND Number Before Making Insulin Dose Decisions

Optimal Insulin Dosing Should Consider:

CGM Number + CGM Arrow + Food + Activity
Now What?

How To Best Use CGM
By Understanding
Dexcom G5 Trend Arrows
What are Rate of Change Trend Arrows?

Direction and velocity of anticipated, changing glucose levels
Anatomy of a Trend Arrow

- Sensor glucose reading and units (mg/dL)
- Trend arrow giving direction and speed of sensor glucose rate of change (steady, increasing, or decreasing)
- Interior color indicates where sensor glucose resides in relation to individual target range
Color Indicates Relation of Current Glucose with Target Range

Ex, 200 mg/dL

120 mg/dL

Ex, 80 mg/dL

65 mg/dL
Dexcom G5: Understanding the UPs and DOWNs

**UPWARD**

- Slowly Rising
  - Increasing 1–2 mg/dL/min
- Rising
  - Increasing 2–3 mg/dL/min
- Rapidly Rising
  - Increasing >3 mg/dL/min

**DOWNWARD**

- Slowly Falling
  - Decreasing 1–2 mg/dL/min
- Falling
  - Decreasing 2–3 mg/dL/min
- Rapidly Falling
  - Decreasing >3 mg/dL/min

**Not increasing or decreasing >1 mg/dL/min**
Usefulness of Rate of Change Arrows

- Directionality of trend arrows allows individuals to “anticipate” future glucose levels

- Information can be used proactively to adjust insulin dose

- Upward trend arrows:
  - Rising glucose levels
  - May suggest need for additional insulin

- Downward trend arrows:
  - Falling glucose levels
  - May suggest a need for less insulin
  - May suggest need for carbohydrate intake
A Simplified Approach to Using Dexcom G5 Trend Arrows
# Not All Arrows Are The Same

<table>
<thead>
<tr>
<th>Trend Arrow Meaning</th>
<th>Dexcom G5</th>
<th>Medtronic 630G/670G</th>
<th>Abbott FreeStyle Libre</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose is rapidly rising Increasing &gt;3 mg/dL/min</td>
<td>↑↑↑↑↑↑↑</td>
<td>↑↑↑↑↑↑↑</td>
<td>—</td>
</tr>
<tr>
<td>Glucose is rising Increasing 2–3 mg/dL/min</td>
<td>↑</td>
<td>↑↑</td>
<td>Glucose is rising quickly &gt;2 mg/dL/min</td>
</tr>
<tr>
<td>Glucose is slowly rising Increasing 1–2 mg/dL/min</td>
<td>→</td>
<td>↑</td>
<td>Glucose is rising 1–2 mg/dL/min</td>
</tr>
<tr>
<td>Glucose is steady Increasing/decreasing &lt;1 mg/dL/min</td>
<td>⇆</td>
<td>→</td>
<td>Glucose is changing slowly &lt;1 mg/dL/min</td>
</tr>
<tr>
<td>Glucose is slowly falling Decreasing 1–2 mg/dL/min</td>
<td>↓</td>
<td>↓</td>
<td>Glucose is falling 1–2 mg/dL/min</td>
</tr>
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<td>Glucose is falling Decreasing 2–3 mg/dL/min</td>
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A Practical Approach to Using Dexcom G5 Trend Arrows

Endocrine Society Approach

• Based on insulin sensitivity ranges for adult and pediatric patients

• For each insulin sensitivity range, dose adjustment in insulin units is recommended

• Insulin adjustments can be simply added or subtracted to standard calculations

• Applicable to MDI or CSII
### Endocrine Society Approach to Using Dexcom G5 Trend Arrows

**ADJUSTING INSULIN DOSES USING TREND ARROWS: PRE-MEAL AND AT LEAST 4 HOURS POST-MEAL**

1. **Patient calculates insulin dose for meal and correction if needed**

2. **Patient looks at the “row” where the correction factor falls**

3. **Patient adds or subtracts insulin dose units to total insulin dose**

<table>
<thead>
<tr>
<th>Arrow Direction</th>
<th>Change in Glucose</th>
<th>Correction Factor</th>
<th>Insulin Dose Adjustment (U)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Rapidly Rising</strong></td>
<td>Increasing &gt;3 mg/dL/min</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>□ less than 25</td>
<td>□ +3.6</td>
<td></td>
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<tr>
<td></td>
<td>□ 25-49</td>
<td>□ +2.5</td>
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<tr>
<td></td>
<td>□ 50-74</td>
<td>□ +2.5</td>
<td></td>
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<tr>
<td></td>
<td>□ over 75</td>
<td>□ +1.5</td>
<td></td>
</tr>
<tr>
<td><strong>Rising</strong></td>
<td>Increasing 2-3 mg/dL/min</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>□ less than 25</td>
<td>□ +3.6</td>
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<td></td>
<td>□ over 75</td>
<td>□ +1.0</td>
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</tr>
<tr>
<td><strong>Slowly Rising</strong></td>
<td>Increasing 1-2 mg/dL/min</td>
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<td></td>
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<tr>
<td></td>
<td>□ less than 25</td>
<td>No adjustment</td>
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<td></td>
<td>□ over 75</td>
<td>No adjustment</td>
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<tr>
<td><strong>Steady</strong></td>
<td>Not increasing/decreasing</td>
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</tr>
<tr>
<td></td>
<td>&gt;1 mg/dL/min</td>
<td>No adjustment</td>
<td></td>
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<tr>
<td><strong>Slowly Falling</strong></td>
<td>Decreasing 1-2 mg/dL/min</td>
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<tr>
<td></td>
<td>□ less than 25</td>
<td>□ -2.5</td>
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<td>□ -1.5</td>
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Endocrine Society Approach to Using Dexcom G5 Trend Arrows

### CLINICAL SCENARIO
- **Food:** 30 g carbohydrate
- **Insulin:Carb Ratio:** 1:10
- **Glucose Target:** 100 mg/dL
- **Correction Factor:** 50 mg/dL/unit

#### STEP 1

1A. Kim divides her carbohydrate by her insulin:carb ratio
\[ 30_\text{g} \div 10 = 3_\text{units} \]

1B. Kim subtracts her target number
\[ 300 - 100 = 200 \]

1C. Kim divides by her correction factor
\[ 200 \div 50 = 4_\text{units} \]

#### STEP 2

Kim subtracts 2.5 units because of the double down arrow
\[ 3_\text{units} + 4_\text{units} - 2.5_\text{units} = 4.5_\text{units} \]
Summary

Using G5 Trend Arrows to Fine-Tune Insulin Doses: The New ‘Standard’ Approach

• This is a starting point; individualize the approach for your patient / family
  • Continue education and refinement with patients

• Insulin stacking will continue to be a challenge

• Goal is to increase time in range; reduce excursions

• Using trend arrows is the new “standard approach” to insulin dosing
Medtronic 670G
Hybrid-Closed Loop

From Research To Real Life Use

The Northwestern Experience
MiniMed 670 G Hybrid Closed Loop

- Only FDA- approved hybrid closed loop system
- Automated basal insulin delivery to a sensor glucose target of 120 mg/dL
- Users need to count carbohydrates and enter them in the bolus wizard prior to meals and snacks
Manual Mode vs. Auto Mode

• In Manual Mode the pump functions like a sensor augmented pump with SmartGuard
  • Threshold suspend “on low” (630G)
  • Predictive threshold suspend “before low” (640G)

• In Auto Mode the basal becomes automated and the rates increase or decrease based on glucose levels
Auto Mode: Boluses

- **Food Bolus**: Programmed carb ratios
  - Food bolus can be accepted or declined, NOT adjusted

- **Correction Bolus**: Suggested is BG > 150 mg/dL
  - Sensitivity factor determined by algorithm
  - Active insulin time programmed in settings
  - Correction target is fixed at 150 mg/dL
  - Correction can be accepted or declined, NOT adjusted
**Medtronic 670G**

**Home Screen in Manual Mode**

**Home Screen in Auto Mode**

**CGM Graph in Manual Mode**

**CGM Graph in Auto Mode**

- New sensor icons
- New Low management suspend icon:
  - Suspend before low
  - Suspend on low
- Auto Basal Deliveries
- Auto Mode shield
**670G Pivotal Trial**

**PIVOTAL TRIAL MINIMED 670G SYSTEM (JAMA 2016)**

**SINGLE-ARM, NON-RANDOMIZED STUDY**

- **10 sites** (9 US, 1 Israel)
- **Type 1 diabetes > 2yrs**
  - A1C <10%
  - Adolescent: 14-21 yrs.
  - Adult: 22-75 yrs.
- **Pump ≥6 months, +/- CGM**
- **Run-in**: Open loop (Manual Mode) 2wks.
- **Study**: Closed loop (Auto Mode) 3mos.
  - 6-day / 5-night hotel stay
  - 24 hour FST (reference i-STAT)

**A1C STUDY RESULTS**

- **Baseline**: ~38% A1C ≤ 7
- **Study**: ~62% A1C ≤ 7

- **A1C**
  - Baseline = 7.4±0.9%
  - Study End = 6.9±0.6%
- **Safety in Study Phase**
  - 0 Severe Hypoglycemia
  - 0 DKA

**Bergenstal RM et al, JAMA 316 (13), 2016**

**Courtesy of Medtronic**
Results - Adults

Run-in Period Manual Mode

Study Period Auto Mode
FreeStyle Flash Libre

- Semi-continuous glucose monitor
- Displays a number/trend arrow
- No alerts/alarms
- Does not communicate continuously with the reader device
- To obtain a real-time glucose number/trend, sensor must be “scanned” with the reader

- Over 400,000 users in Europe (2 hours warm up and 14 days wear)
- Just released late December 2017 (US 12 hours warm up and 10 days wear)
- Approved by CMS (Jan 2018)
Freestyle Libre Sensor

- Factory Calibrated, disposable
- Small size (2 stacked quarters)
- Wear for up to 10 days
- No finger prick calibrations, unless reader asks to check BG
- Water resistant ok for shower and exercise
- Not affected by Acetaminophen
- Affected by Aspirin and Vitamin C
Reader Provides Multiple Reports

**Daily Patterns (mmol/L)**

- Last 14 Days

**Time In Target**

- Above: 34%
- In Target: 54%
- Below: 12%

Target Range: 4.4-10.0 mmol/L

**Low Glucose Events**

- Total Events: 10
- Day 0: 1
- Day 12: 3
- Day 24: 6

**Last 14 Days**
Guardian Connect Mobile CGM with Guardian 3

- Stand alone CGM
- Medtronic Guardian 3
- Phone App on IOS only
- No sharing features
- Approved for ADJUNCTIVE use only
Dexcom G6

- Approved March 26th 2018
- Class II, integrative CGM
- NO calibrations
- Sensor life 10 days
- No acetaminophen interference
Smaller Transmitter & Auto Applicator
Eversense (Senseonics) Implantable Sensor
Doctor’s Office Insertion

1. Make incision
2. Create subcutaneous pocket
3. Insert sensor
4. Close incision

- 5-8 mm incision upper arm (Lidocaine)
- Approximately 3-5 mm below skin surface
- Sensor placed with custom inserter
- Steri-Strips™ to close
Smart Pens!
InPen

- Available for Novolog OR Humalog
- Half Unit increments
- Future integration with Dexcom G6 and I-Health (iOS)
InPen APP

Snapshot
Dose Calculator
LogBook
Progress Reports
Alerts and Reminders
Future Smart Pens

Esysta, smart insulin pen available in Germany

GoCap- smartphone connected insulin pen cap

Smart-phone connected insulin pen cap (from the inventors of Timesulin cap)

InsulCheck smartphone-connected insulin pen wraparound
Timelines as of 10/12/2017:
- Feasibility study completed in August 2016
- Pivotal study planned to complete by end of 2017
- Launch goal: Summer 2018
OmniPod Dash

BLE Pod

BLE Blood Glucose Meter

PDM (Android Locked-Down Device)
Open APS Models

Continuous glucose monitor
Battery
Raspberry Pi
Insulin pump
@DanaMLewis
#OpenAPS

Nightscout (optional)
CGM

AW, or other watch (optional)

USB battery pack
Raspberry Pi portable computer

Dexcom CGM receiver

CareLink USB stick

Northwestern University
Feinberg School of Medicine
Bigfoot, I-llet And UVA Future CL Systems
Thank You