Diabetes Technology: Pumps and CGM

1st Annual Sweet Science Conference
10/7/17

Bryce Nelson, MD/PhD
Associate Professor, Clinical Pediatrics
University of South Carolina School of Medicine-Greenville
Medical Director, Division of Pediatric Endocrinology
Disclosures

- Dexcom, Speakers Bureau
Learning Objectives

• To Understand the use of insulin pumps and CGM to improve patient outcomes in diabetes management
  – Insulin Pump
    • Types
    • Utility in diabetes care
    • Current outcomes with insulin pumps in diabetes
  – CGM
    • Types
      – Professional vs Therapeutic CGM
      – Utility in Diabetes
      – Current outcomes
      – Pump integration
      – Artificial Pancreas
Clinical Centers

N = 67

Types of Patients

- Adult: 18
- Pediatric: 37
- Both: 12

Setting

- Institution: 52
- Community: 14
- Managed Care: 1

T1D Exchange
Clinical Centers
Age Distribution

N = 20,110

<table>
<thead>
<tr>
<th>Age (Years)</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;6</td>
<td>947</td>
</tr>
<tr>
<td>6-12</td>
<td>5481</td>
</tr>
<tr>
<td>13-17</td>
<td>5032</td>
</tr>
<tr>
<td>18-25</td>
<td>2867</td>
</tr>
<tr>
<td>26-49</td>
<td>3508</td>
</tr>
<tr>
<td>≥ 50</td>
<td>2275</td>
</tr>
</tbody>
</table>
Demographics

Gender
- Female: 50%
- Male: 50%

Race/Ethnicity
- White: 83%
- Asian: 5%
- Black: 1%
- Other: 3%
A1c...we don’t meet target
Excellent versus Poor Control

Excellent control group (HbA1c \(\leq 7.0\%\)) differed from poor control group (HbA1c \(\geq 9.0\%\)) in:

- more often using insulin pumps
- more frequent self-monitoring of blood glucose
- missing fewer insulin doses
- bolusing before meals rather than at the time of or after meal
- using meal specific insulin:carbohydrate ratios
Severe Hypoglycemia in Adults by T1D Duration

Seizure or loss of consciousness

Diabetes Duration
- <20 years
- 20-<40 years
- ≥40 years

Age, yrs
- 31-<50
- 50-<65
- ≥65

- 8%
- 12%
- 22%
- 8%
- 13%
- 17%
- 7%
- 16%
- 21%
Insulin pump history

• **1963**: The first prototype of a 'pump' that delivered glucagon as well as insulin was similar to a backpack and was developed by Dr Arnold Kadish.

• **1973**: Dean Kamen invented the first wearable infusion pump.

• **1976**: AutoSyringe Inc begin to manufacture and market the pumps Dean Kamen invented.

• **1976**: Development of continuous subcutaneous insulin infusion begins (insulin pump therapy).

• **1980s**: BioStar glucose controlled insulin infusion system used- functioned as an artificial pancreas.

• **1990s**: First Medtronic MiniMed pump released.

• **2012**: Trials of artificial pancreas' begin in the USA.
Insulin Pump Use

- In 2005, estimated that 20-30% of T1D and <1% of insulin treated T2D patients are using insulin pumps
  - 350,000 – 515,000 users in US
- Currently no official requirement for medical supervision
- No unified certification process
Insulin Pump Use in Diabetes

• Advantages
  – Can be used in any type of diabetes
  – Efficient Insulin delivery
  – Tends to be associated with lower A1c
  – Ease of fine titration
  – Flexible
  – Convenience
  – Programmable
    • Individualized, variable basal rates
    • Carb ratio, correction factor programming
  – Meter Linkage
  – Cost effectiveness in T1D and T2D
Insulin Pump Use in Diabetes

• Disadvantages
  – Complex
  – Requires additional skill
  – Prone to failure
  – Who is the right candidate?

• Indications
  – Severe, recurrent hypoglycemia
  – Hypoglycemic Unawareness
  – Extreme Insulin Sensitivity
Who is a good candidate for Insulin pump therapy?

- A patient with T1DM or intensively managed insulin-dependent T2DM
- Currently performing ≥4 insulin injections and ≥4 self-monitored blood glucose (SMBG) measurements daily
- Motivated to achieve optimal blood glucose control
- Willing and able to carry out the tasks that are required to use this complex and time consuming therapy safely and effectively
- Willing to maintain frequent contact with their health care team

AACE/ACE Joint Consensus Statement. 2014
Who is a good pump candidate?

- **Adult patients**
  - At CSII initiation, the patient should have daily contact with the pump trainer
  - A return visit with the endocrinologist/diabetologists/advanced practice nurse is advised within 3 to 7 days of initiation
  - Educational consults should be scheduled weekly or biweekly at start, then periodically as needed
  - Specialist follow-up visits should be scheduled at least monthly until the pump regimen is stabilized, then at least once every 3 months

- **Pediatric patients**
  - An international consensus conference of leading pediatric diabetes specialists agreed that CSII was indicated for pediatric patients with:
    - Elevated hemoglobin A1c (HbA1c) levels on injection therapy
    - Frequent, severe hypoglycemia
    - Widely fluctuating glucose levels
    - A treatment regimen that compromises lifestyle
    - Microvascular complications and/or risk factors for macrovascular complications
CMS Insulin Pump Eligibility Criteria

- Must meet 1 of the following:
  - Completed comprehensive diabetes education program and received MDI insulin with frequent self-adjustment for at least 6 months with documented SMBG frequency of ≥4 X daily for previous 2 months. Must also meet ≥1 of the following:
    - A1c > 7.0%
    - History of recurrent hypoglycemia
    - Wide fluctuations in blood glucose before meals
    - “Dawn Phenomenon” with FPG frequently >200 or history of severe glycemic excursion
  
- Patient on pump therapy before enrollment with a documented SMBG an avg of ≥4X daily one month prior to enrollment

- Fasting C peptide ≤ 110% lower limit of normal or ≤ 200% lower limit of normal if CrCl ≤50 ml/min with concurrent FBG ≤225, or +diabetes autoimmunity
Does insulin pump therapy improve care?

• Most studies have shown:
  – Compared basal/bolus MDI to CSII showed insulin pump use to be associated with improved A1c
  – Improved quality of life
  – No difference in body weight
  – Reduction of severe hypoglycemia

• STAR-3 Trial
  – Better A1c with sensor augmented pump therapy compared to conventional basal bolus MDI
I have identified a good candidate…now what?

- Keys to success
  - Extensive Education
    - Pump troubleshooting
    - Extensive review of pump technology and mechanics
    - Proper Catheter insertion and placement technique
    - Frequent BG monitoring
    - Meaning of Pump alarms
    - Pump failure protocol
    - On call availability for patients
    - Understanding of pump warranty
    - Retesting knowledge base periodically after initial pump training
Insulin pump types (FDA approved)

Medtronic 630G/670G

Omnipod

Tandem T-Slim

Animas Vibe

V-Go
Medtronic 630/670G

Unique Advantages
• Large, secure, long-established company
• Industry leader in R & D
• Pump comes with integrated Enlite CGM system; data displayed on pump screen
• Automatic basal shutoff when low glucose detected by sensor (may help prevent severe hypos)
• Optional “Connect” feature for sharing CGM data with smartphones (not available for 670G)
• Quick/simple bolus programming
• Slim/streamlined attachable clip
• Accepts radio communication from multiple blood glucose meters
• Easily downloadable to online Carelink program
• Can set I:C ratios in .1g increments
• Generates insulin/carb/BG statistics

Potential Drawbacks
• Not water-tight but improved in 670G
• Must use proprietary infusion set tubing
• Slow bolus delivery
• No food database
• Must pay for loaner/backup pumps
• Holds 180 units; 300-unit version is slightly larger
• Insulin-on-board only deducted from correction boluses
• Duration of action set in whole-hour increments
• CGM & pump alerts may not be loud enough for some to hear
• Data from pump/CGM not downloadable to any program other than Carelink & Carelink Pro
• (working on Glooko availability)

*integrateddiabetes.com
Omnipod

Unique Advantages
• Reduced up-front costs
• Can program through clothing from a few feet away
• Discrete pump size (compared to other pumps)
• No tubing (minimizes wasted insulin, no tangling/snagging, less awkward, no air pockets, no siphoning effects)
• No disconnecting/reconnecting means no missed/lost insulin
• Simple, automated canula insertion minimizes pain, reduces “human errors”, creates more site options
• Forced pod change reduces chances for lipodystrophy & absorption problems
• Pump is fully watertight
• Temp basals and boluses can be customized/preset
• Freestyle meter built into handheld programmer
• Can customize programming text without PC linkup
• Large color screen w/full-sentence text and graphing capability
• Only 2 parts; convenient for travel

*integrateddiabetes.com

Potential Drawbacks
Somewhat bulky programmer
Pod creates a “bulge” on the skin
Cannot enter boluses or make setting changes without programmer
Cannot do programming or editing while bolus is delivering
Only one canula orientation/length; may not work for all body types
Max reservoir volume 200u; minimum fill amount 85u
Pod stops working after 72 hours (plus grace period)
Handheld will not calculate bolus if BG < 50
Dislodged/clogged canula requires complete pod replacement
“Disconnection” requires complete pod replacement
Pod does not have vibrate option
Must suspend when changing basal settings
Temp basal limited to 12 hours max
Not covered by all 3rd party payors
Insulin-to-carb ratios in whole-numbers increments only
Loss (or malfunction) of remote/PDM renders pod non-programmable (delivers basal only)
Tandem T-Slim

Unique Advantages

• Bright, full-color touch screen
• Modern, high-tech appearance
• Compact, thin dimensions
• Rapid numeric entry, fastest bolus entry
• Cartridges hold 300u (t:slim); 480u (t:flex)
• Can calculate boluses up to 50 units (60 on t:flex)
• Site-change reminder w/customizable day & time
• Graphic on-screen history display
• Carb counting calculator
• Temp basal up to 250%, 72 hrs
• Can set duration of insulin action in 1-minute increments
• IOB & time remaining displayed on home screen
• Missed bolus reminders customizable by day of week
• Alert for high temperatures which may spoil insulin
• Secondary basal programs linked with secondary bolus calculation parameters
• Web-based download software
• Compatible w/leur-lock infusion sets
• Minimal insulin movement with changes in altitude

Potential Drawbacks

• Small buttons can be difficult to activate; screen goes blank if buttons missed 3x
• Unlock procedure required to perform any programming
• No integrated clip (must put in a case that has a clip)
• Tubing connector looks “medical,” can snag on clothing
• Basal & bolus settings in same time slots; may take several steps to edit
• Extra confirmation steps with all programming
• Weak vibrate mechanism
• No meter link
• Manufacturer relatively new in pump industry
• Requires charging 1-2x/week
• No formal in-warranty upgrade policy

*integrateddiabetes.com
Animas Vibe

Unique Advantages
• Displays data from Dexcom G4 CGM
• 35-Unit maximum bolus
• Fully water-tight
• Very bright, full-color screen; easy to read
• Superior dosing accuracy (esp. at small doses)
• AA Lithium battery lasts 6-8 weeks
• User-defined timeout setting
• User-defined occlusion sensitivity
• User-defined bolus delivery rate
• Customizable tune for alerts
• Cartridges very easy to fill without air bubbles
• Pump and CGM data downloadable to Diasend web-based software
• Strong integrated metal clip

Potential Drawbacks
• Does not link with blood glucose meter
• Utilized older-generation Dexcom data algorithm
• Battery change requires re-priming
• Insulin-to-carb ratios in whole-number increments only
• Cannot see cartridge inside pump
• Extra button presses required with most standard programming
• No data averages or statistics generated on pump screen
• Cannot recall blood glucose or carb history on pump screen
• Insulin On-Board is not subtracted uniformly from boluses
• 200-Unit cartridge limit
• Cursor (scroll) speed difficult to master
• Bolus delivery may be too rapid for those taking large doses

*integrateddiabetes.com
Continuous Glucose Monitoring

- Designed to improve control without the addition of more medication.
- First attempted in 1967 by Updike and Hicks
- 1999: Glucowatch
AHHH... THE FIRST LAWN MOWING OF SPRING, WHEN HE RECYCLES ALL THOSE LEFTOVER GLUCOSE STRIPS FROM WINTER AND TURNS THEM INTO MULCH...
Types of CGM

- Dexcom G5
- Eversense
- Libre
- Medtronic Enlite 3
- Glyssens
CGM Use in T1D Exchange

- Analysis included 12,088 clinic registry participants who had completed a year 1 follow-up visit
  - CGM use defined as using real-time CGM during the past month
  - 1,089 CGM users and 10,999 non-CGM users
  - Median duration of CGM use: ~1.5 years
48% of CGM users <18 years old use Dexcom.
Several Studies Support Improved Glycemic Control in DM with CGM

- **Star-1**
  - 12-72 years of age
  - >60% CGM use associated with improved A1c

- **JDRF**
  - 15-25 years of age
  - Improved A1c with CGM use compared to SMBG alone
  - Rare severe hypoglycemic events
  - Frequency of CGM use associated with greater improvements in A1c

- **DirecNet & JDRF CGM**
  - 13 week and 26 weeks, 8-14 years
  - Improved A1c
  - Lower rate of hypoglycemia
Mean HbA1c by CGM Use

- Non CGM Users
- CGM Users

<table>
<thead>
<tr>
<th>Age, years</th>
<th>Non CGM Users</th>
<th>CGM Users</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;13</td>
<td>8.2%</td>
<td>7.8%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>13-&lt;26</td>
<td>8.6%</td>
<td>8.1%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>≥26</td>
<td>7.6%</td>
<td>7.2%</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

(N=2,986)(N=159) (N=4,281)(N=208) (N=1,882)(N=450)
Mean HbA1c by CGM Use Frequency

P<0.001

Mean HbA1c %

CGM Use Frequency

<3.5 d/wk (N=179) 7.9%

3.5-6 d/wk (N=151) 7.6%

≥6 d/wk (N=427) 7.3%
# CGM Use in Youth and Young Adults in T1D Exchange

## Table 1: Participant Characteristics

<table>
<thead>
<tr>
<th></th>
<th>2010-2012</th>
<th>2015-2016</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age - mean±SD (yrs)</td>
<td>14±5</td>
<td>15±5</td>
</tr>
<tr>
<td>Age - N(%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;6 years</td>
<td>676(4%)</td>
<td>506(4%)</td>
</tr>
<tr>
<td>6-&lt;13 years</td>
<td>5341(35%)</td>
<td>3700(27%)</td>
</tr>
<tr>
<td>13-&lt;18 years</td>
<td>5591(36%)</td>
<td>5780(43%)</td>
</tr>
<tr>
<td>18-&lt;26 years</td>
<td>3753(24%)</td>
<td>3488(26%)</td>
</tr>
<tr>
<td>Gender – Female N(%)</td>
<td>7480(49%)</td>
<td>6109(49%)</td>
</tr>
<tr>
<td>White Non-Hispanic N(%)</td>
<td>12053(79%)</td>
<td>10591(79%)</td>
</tr>
<tr>
<td>Private Insurance - N(%)</td>
<td>9689(73%)</td>
<td>9448(74%)</td>
</tr>
<tr>
<td>Diabetes Duration - mean±SD (yrs)</td>
<td>6±5</td>
<td>8±4</td>
</tr>
<tr>
<td>Pump Users - N(%)</td>
<td>8446(55%)</td>
<td>8262(62%)</td>
</tr>
<tr>
<td>CGM Users - N(%)</td>
<td>530 (3%)</td>
<td>2377(18%)</td>
</tr>
</tbody>
</table>

*Miller, K, et al. Continuous Glucose Monitoring (CGM) Use in Type 1 Diabetes: An Update from the T1D Exchange Clinic Registry. ADA Poster, 2016*
CGM Use is on the rise and associated with lower A1c

*Miller, K, et al. Continuous Glucose Monitoring (CGM) Use in Type 1 Diabetes: An Update from the T1D Exchange Clinic Registry. ADA Poster, 2016*
Real Time CGM Use Led to Reduction in HbA1c at 6 Months Through 18 Months for Patient with >7% HbA1c

The Reduction In A1c Is Directly Correlated with Frequency of Sensor Use

---

Time Spent in Hypoglycemia Significantly Reduced with CGM

Frequency of CGM Glucose Levels ≤ 70, ≤ 60 and ≤ 50 mg/dL

Each comparison Baseline vs 13 and 26 wks

Diabetes Care 2009: 32:1378-1383
Is CGM only helpful in pump users or can it be used in patients on basal/bolus MDI?

You betcha!!!!
Study Objective

Determine the impact of CGM for patients using multiple daily injections (MDI)

Study Design

Independent randomized, controlled trial - 24 weeks

158 T1D subjects

Similarly powered design to STAR 3 and JDRF

Minimal training and follow up to mimic real-life care
**Primary Outcome**

HbA1c reduction of 0.9% from baseline in CGM group and reduction of 0.6% compared to control at 24 wks

**Secondary Outcomes**

- Subset of subjects with HbA1c > 8.5% (uncontrolled) had a 1.3% reduction in HbA1c at 24 weeks
- CGM group spent 101 more minutes/day in target range than the control group
- CGM group experienced a 30% reduction from baseline in time spent low <70 mg/dL
- CGM group experienced a 30% reduction from baseline in time spent high >250 mg/dL
- CGM group experienced statistically significant less time spent <60 mg/dL overnight than control

**Important Note:** The study demonstrated no impact to outcomes based on differences in age, literacy, education or numeracy.
Other Observations

SMBG frequency reduced from 5.1 to 3.6 times/day

89% of the subjects wore CGM ≥ 6 days per week (near daily use)

Study Significance

First RCT to ever assess and determine the clinical benefits of CGM with MDI

Study results clearly demonstrate that MDI patients will wear and benefit from CGM and it should be considered the first tool prescribed to gain better glucose control
Study Objective
Comparison of different treatment modalities for Type 1 diabetes including Sensor Augmented Insulin Regimens (SAIR)

**Study Design**
- Prospective study analysis
- 65 adult T1D subjects
- Divided into three groups based on treatment modalities
- Followed up for 52 weeks

**Treatment Modalities**
- 18 Control – MDI + SMBG
- 20 CSII (no CGM)
- 27 SAIR (Sensor Augmented Insulin Regimens)
  - 15 CSII + CGM
  - 12 MDI + CGM
COMISAIR

**Glycated hemoglobin (%)**

- **MDI+SMBG**
- **PUMP+SMBG**
- **SAIR** Both MDI+CGM and PUMP+CGM

- ▲ Both sensor-augmented insulin regimens
- ■ Insulin pump therapy
- ● Multiple daily injection therapy

**Months**

0 3 6 9 12
A1C Impact

Graph showing the impact of insulin pump therapy (without real-time CGM), multiple daily injection + real-time CGM, and sensor-augmented pump therapy on glycated hemoglobin levels at baseline, 3 months, 6 months, 9 months, and 12 months. The graph indicates a significant difference in the 9-month and 12-month data points compared to baseline and previous time points.
Sensor Accuracy makes it possible

Bailey T. et al Journal Diabetes Science and Technology. 2015 March; 9(2); 209-214
Professional vs Personal CGM Use

• Professional: CGM is owned by provider
  – Worn by patient for 3-5 days
  – Blinded vs unblinded
  – Downloaded and analyzed by patient
  – Billable
    • CPT for insertion (95250), and interpretation (95251)
Candidates for CGM

- No specific algorithm yet to identify patients
- Every person with diabetes?
- T1D
  - Hypoglycemic unawareness or frequent hypoglycemia
  - A1c above target
  - Excessive glycemic variability
  - Requires A1c lowering without increased hypoglycemia
- Children or Adolescents with T1D and A1c <7.0
- Youth with T1D and A1c of >7.0 and able to wear it nearly on a daily basis

AACE consensus statement. 2010
Therapeutic CGM

- Recent FDA ruling for Dexcom 12/16
  - Only sensor approved for therapeutic CGM
  - Replacement for fingerstick BG

- Accuracy
- Alerts
- Trends

FEATURES

Alerts & Alarms:
Alerts including a built-in hypo alarm (55 mg/dL) warn of glucose highs and lows, allowing user to take appropriate action.

Data Sharing:
Via the Dexcom G5 Mobile App, users can share their glucose information with up to five individuals for added support. (Requires the Dexcom Follow App®)

Frequent Readings

24 hours/day
UP TO 88 READINGS A DAY
EVERY 5 MINUTES
Alerts: Spending less time in hyperglycemia or hypoglycemia

- Minimize the duration of BG outside target range

*Schiener, G. Making the Most out of Continuous Glucose Monitoring*
Treatment Decisions based on Trend Arrows

 Dexcom G5 mobile
 Treatment Decisions: Advanced for use by Healthcare Professionals

The Dexcom G5® Mobile Continuous Glucose Monitoring (CGM) System can help optimize diabetes treatment plans. Use a correction factor and add or subtract the number the arrow represents.

Start with these resources to help guide the conversation with your patients about using the Dexcom G5 Mobile for treatment decisions:
- Dexcom G5 Mobile Treatment Decisions: The Basics: dexcom.com/fingersticks
- Dexcom G5 Mobile CGM System User Guide: dexcom.com/guides

What do the arrows mean?

- Glucose could increase more than 90 mg/dL in 30 minutes.
- Glucose could increase 60-90 mg/dL in 30 minutes.
- Glucose could increase 30-60 mg/dL in 30 minutes.
- Steady. Not increasing/decreasing more than 1 mg/dL each minute.
- Glucose could decrease 30-60 mg/dL in 30 minutes.
- Glucose could decrease 60-90 mg/dL in 30 minutes.
- Glucose could decrease more than 90 mg/dL in 30 minutes.

Possible Adjustments:

- Current glucose plus 100 mg/dL.
- Current glucose plus 75 mg/dL.
- Current glucose plus 50 mg/dL.
- No adjustment.
- Current glucose minus 50 mg/dL.
- Current glucose minus 75 mg/dL.
- Current glucose minus 100 mg/dL.

This is a summary of a clinical article published in a peer reviewed journal. This method should only be used for pre-meal and correction dosing. Correction dosing should be at least two hours after last insulin dose.

Kim has a target glucose of 100 mg/dL and a correction factor of 1:50. This means she would take 1 unit of rapid-acting insulin to lower her glucose about 50 mg/dL. Let's see what Kim does:

<table>
<thead>
<tr>
<th>Glucose Level</th>
<th>Adjustments</th>
<th>Calculation</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>225 mg/dL</td>
<td>+75</td>
<td>225 + 75</td>
<td>225</td>
</tr>
<tr>
<td>300 mg/dL</td>
<td>-100</td>
<td>300 - 100</td>
<td>200</td>
</tr>
</tbody>
</table>

Kim adds 75 mg/dL because of the up arrow.
Kim subtracts her target number.
Kim divides by her correction factor.
Kim uses her insulin pen to take 4 units of insulin.

If Kim had an insulin pump, she would input 300 mg/dL and let the pump do the math.

Whether your patients are new to Dexcom or experienced, they should keep using a meter to make treatment decisions until they know how Dexcom works. Don’t rush it! It may take days, weeks or months for your patients to gain confidence in using Dexcom G5 Mobile to make treatment decisions. They should keep confirming glucose readings with a meter until they understand:

- the accuracy experienced with each newly inserted sensor may vary
- a sensor might work differently in different situations (meals, exercise, first day of use, etc.)
Dexcom and Medicare

• In 2017, The Centers for Medicare and Medicaid Services (CMS) Medicare made a milestone Ruling, establishing benefit coverage for “therapeutic” CGM—a designation applying only to those CGM systems approved for use in making diabetes treatment decisions without a fingerstick (“non-adjunctive use”). The Dexcom G5® CGM System is the only therapeutic CGM system covered as a Medicare benefit.

• Coverage Requirements
To qualify for Medicare coverage of therapeutic CGM, beneficiaries need to meet the following individual claim criteria:
  – Beneficiary has diabetes mellitus; and,
  – Has been using a home blood glucose monitor (BGM) and performing BGM testing four or more times a day; and,
  – Is insulin-treated with multiple daily insulin injections (MDI) or on an insulin infusion (CSII) pump; and,
  – Beneficiary's insulin treatment regimen requires frequent self-adjustment based on therapeutic CGM results.
  – Patients must meet all of the requirements outlined above to be eligible for coverage.

• Prescribing Information
To prescribe the Dexcom G5 for a Medicare beneficiary, you will need to complete a Certificate of Medical Necessity (CMN). The CMN must include the following documentation:
  – The beneficiary requires a therapeutic CGM
  – The beneficiary has diabetes mellitus; and,
  – The beneficiary has been using a home blood glucose monitor (BGM) and performing frequent (four or more times a day) BGM testing; and,
  – The beneficiary is insulin-treated with multiple daily injections (MDI) of insulin or a continuous subcutaneous insulin infusion (CSII) pump; and,
  – The beneficiary's insulin treatment regimen requires frequent adjustment by the beneficiary on the basis of therapeutic CGM testing results.
WE MADE IT TO
THE TOP!
LOOK AT THAT
SPECTACULAR VIEW!!

LOOK AT THAT
SPECTACULAR
BLOOD GLUCOSE!
Artificial Pancreas

Insulet's Horizon Artificial Pancreas Based on the Omnipod Dash System Mobile Platform

All Dash Features
- Sameday only
- Smarter with on-body analytics
- PHSO (patient health self-observation)
- New CGM (Continuous Glucose Monitoring) data via secure direct connect

BIONIC PANCREAS

beta bionics
www.bionicsconnections.com

bigfoot Biomedical

collaborates with Abbott
Closed Loop Progression

- 1990s: Insulin pump advocated for use in children
- 2000s: RT Glucose Sensors
- 2008: Weinzimer et al., pediatric 34 hours closed loop
- 2010: O’Grady, et al., 2 nights
- 2013: Phillip, et al., 1 night, pediatric
- 2014: Russell, et al., Bionic Pancreas (bihormonal), 5 days, adults and kids
- 2015: Ly, Buckingham, et al., 6 days; Thabit et al., Adults, 3 months
- 2016: Medtronic 670G Pivotal Trial (JAMA), 3 months, Adults and kids
- 2017: Medtronic 670G FDA approved as first hybrid closed loop device
Medtronic 670G Features

- First commercially available hybrid closed loop system
- 14 years and older
- April 2017
- Looks similar to 630G
  - Color screen
  - 300U reservoir
- Enlite 3 Sensor
  - Enhanced accuracy
  - 7 day wear
  - Only sensor approved to drive insulin delivery
- Designed to ”treat to target”
  - 120 mg/dl and 150 mg/dL
Medtronic 670G Features

SMARTGUARD™ HCL TECHNOLOGY
LESS WORRY, MORE TIME IN RANGE

SmartGuard™ HCL technology is an insulin pump technology that automatically adjusts insulin delivery based on sensor glucose readings. The technology offers multiple options to meet the needs of different people with diabetes.

### Auto Mode
- Basal insulin delivery is automatically adjusted throughout the day and night to a target of 120 mg/dL
- Basal insulin delivery determined by our new Guardian Sensor 3
- Target can be temporarily set to 150 mg/dL for exercise and other events
- Carb and BG entry is needed for meals
- Need to calibrate the sensor

### Predictive Mode Options
- Suspend before low: Pump temporarily stops delivering insulin if the SG value is approaching the Low Limit set
- Suspend on low: Pump temporarily stops delivering insulin if the sensor value reaches or falls below pre-set low limit. (Also in MiniMed 530G and MiniMed 630G)

MiniMed systems are still the only ones in the world that take action.
Medtronic 670G Pivotal Trial Results

- 3 month, 124 subjects >14 years
- 0.5% reduction in A1c (drop from 7.4% to 6.9%)
- 44% reduction in time spent with low blood glucose (<70 mg/dl)
- 40% reduction in time spent in severe hypoglycemia (<50 mg/dl)
- 11% reduction in time spent over 180 mg/dl
- 8% improvement in time spent in range (71-180 mg/dl)

- Of the 124 patients in the trial, 80% continued on the device through the FDA’s continued access program
- Not a randomized study

Garg, SK et al. DTT. 2017.
Adults on 670G

Garg, SK et al. DTT. 2017.
Adolescents on 670G

Garg, SK et al. DTT. 2017.
## Medtronic 670G Pivotal Study

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Adolescents Age &lt;21 (N = 30)</th>
<th>Adults Age &gt;21 (N = 94)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age-year</td>
<td>16.5 ± 2.29</td>
<td>44.6 ± 12.79</td>
</tr>
<tr>
<td>Diabetes Duration - years</td>
<td>7.7 ± 4.15</td>
<td>26.4 ± 12.43</td>
</tr>
<tr>
<td>Total daily insulin Dose – U/kg/day</td>
<td>0.8 ± 0.24</td>
<td>0.6 ± 0.20</td>
</tr>
<tr>
<td>HbA1c% at screening</td>
<td>7.7 ± 0.84</td>
<td>7.3 ± 0.91</td>
</tr>
</tbody>
</table>

### Medtronic 670G Pivotal Study

<table>
<thead>
<tr>
<th></th>
<th>Run In (Baseline)</th>
<th>3 month Data</th>
</tr>
</thead>
<tbody>
<tr>
<td>HbA1c</td>
<td>7.4± 0.9</td>
<td>6.9± 0.6</td>
</tr>
<tr>
<td>% &lt; 70 mg/dl</td>
<td>6.4 ± 5.3</td>
<td>3.3 ± 2.0</td>
</tr>
<tr>
<td>% &lt; 50 mg/dL</td>
<td>1%</td>
<td>0.6%</td>
</tr>
<tr>
<td>% 71 - 180</td>
<td>66.7 ± 12.2</td>
<td>72.2 ± 8.8</td>
</tr>
<tr>
<td>Mean Glucose</td>
<td>150 mg/dl</td>
<td>151 mg/dl</td>
</tr>
<tr>
<td>Sensor Wear</td>
<td></td>
<td>95%</td>
</tr>
<tr>
<td>Time in Auto Mode</td>
<td></td>
<td>87%</td>
</tr>
<tr>
<td>TDI</td>
<td>47 ± 22</td>
<td>51 ± 27</td>
</tr>
</tbody>
</table>

4 NIGHTS IN A SINGLE WEEK OF A PATIENT
GLUCOSE AND INSULIN FROM 12:00 AM TO 7:00 AM
Artificial Pancreas: The Future
Beta Bionics: iLet

- Bihormonal
  - Insulin & Glucagon
  - Multicenter study
    - 39 Adults (>18 years)
    - 11 day closed loop
    - Mean CGM Control: 162 ± 29
      - Time < 60: 1.9%
      - Time > 180: 34%
    - Mean CGM Bihorm: 141 ± 10
      - Time < 60: 0.6%
      - Time >180: 20%
Artificial Pancreas: The Future
Beta Bionics: iLet

• Bihormonal
  – Insulin & Glucagon
  – 2013 Summer Camp Study
    • 32 teens (12-20 years)
    • 5 day closed loop
    • **Mean CGM Control: 158 ± 27**
      – Time <60: 2.2%
      – Time >180: 31%
    • **Mean CGM Bihorm: 142 ± 12**
      – Time < 60: 1.3%
      – Time >180: 21%
Artificial Pancreas: The Future
Beta Bionics: iLet

- Bihormonal
  - Insulin & Glucagon
  - 2016 Summer Camp Study
    - 19 Pre-teens (6-11 years)
    - 5 day closed loop
    - Mean CGM Control: 168 ± 30
      - Time < 60: 2.8%
      - Time > 180: 36%
    - Mean CGM Bihorm: 137 ± 11
      - Time < 60: 1.2%
      - Time > 180: 17%

- Pivotal Trials to begin 2018
Bionic Pancreas Results

2013 Summer Camp Study: Summer 2013
32 Teens (12–20 years)
5-Day Experiments

2014 Summer Camp Study: Summer 2014
19 Pre-Teens (6–11 years)
5-Day Experiments

Bionic Pancreas Multi-Center Study: Q2 2014 – Q2 2015
39 Adults (≥ 18 years)
11-Day Experiments
THE LEGEND OF BIGFOOT

ARE WE EVER GOING TO SLEEP AGAIN?

This was the simple question that started Bryan Mazlish on the path to his revolutionary diabetes technology development. Though Bryan’s wife had lived with T1D for many years, it wasn’t until their son Sam’s diagnosis at age 5 that Bryan truly understood the complexity of managing T1D. He was handling their son’s nighttime care and waking every three hours to monitor Sam’s blood glucose levels. The amount of work was staggering, and no matter how focused he was, he carried a heavy weight of worry.

From his career in finance and automated stock trading, Bryan had learned that, in the right circumstances, a machine can by and large make better decisions than humans if given the appropriate information and direction. The machines never tire, never get distracted. With this mindset, Bryan began teaching himself about insulin and carb absorption and applied his experience with quantitative trading algorithms to create models to predict future blood sugar trends. He set about creating remote monitoring tools similar to, but pre-dating, the Nightscout CGM in the Cloud movement, using the Dexcom SEVEN® PLUS system available at the time. He studied the academic research on artificial pancreas development. With his wife Sarah, a medical doctor, right there to provide instant feedback after each development cycle, his speed of iteration was incredible.

A BETTER SOLUTION

BRYAN HAD ASKED SARAH WHAT HE COULD DO TO MAKE HER LIFE WITH T1D EASIER. WHAT SHE TOLD HIM WAS CLEAR AND POWERFUL, AND IT GUIDED HIS DEVELOPMENT PROCESS:

“If I could wake up every morning with a perfect blood sugar, life would be so much better.” Bryan’s system achieved that for both Sarah and Sam, and it also reduced blood sugar spikes and dips throughout their daily lives. “I was immediately and unequivocally sold,” Sarah recalls. “The system gave me back mind space by taking over the micromanagement of my blood sugar.”

AFTER SPEAKING WITH FDA ABOUT HOW TO BRING THEIR TECHNOLOGY TO A BROADER AUDIENCE, BRYAN WAS DETERMINED TO FIND A COMMERCIAL PARTNER. FOR TWO YEARS, HE SHOPPED HIS TECHNOLOGY TO ALL THE POTENTIAL SUITORS.

“I WAS ESSENTIALLY WILLING TO GIVE IT AWAY,” HE SAYS, BUT CONVERSATIONS MOVED SLOWLY.

THERE SEEMED TO BE A BASIC MISUNDERSTANDING WITHIN THE INDUSTRY ABOUT WHAT AUTOMATED INSULIN DELIVERY REALLY IS - NOT A FEATURE TO BE ADDED TO AN EXISTING PUMP, BUT A COMPLETE CHANGE TO THE PARADIGM OF CARE.
Bigfoot Biomedical

- Asante Pump body integrated with controller
- Talks to CGM (Libre) with control algorithm
- Smartphone Interface
- Initial study completed 12/16
- Pivotal Trial coming soon
Tandem T Slim X2

- Predictive low glucose suspend integrated into X2 with Dexcom G5 integration
  - Software download
  - 90 subject pivotal trial starting soon with FDA approval possibly 2018
- Automated Insulin Delivery in collaboration with TypeZero
  - Pivotal study as a part of the International Diabetes Closed Loop (iDCL) Trial led by Univ of VA
Omnipod Horizon™ Automated Glucose Control System

- 6 preliminary studies with meal and exercise challenges
- 82 participants: adults, adolescents, and children
- Preliminary data for hybrid closed loop
  - Mean glucose 136-153 mg/dL
  - 60% less time with BG > 70 compared to run in phase
  - Time in range 85%
  - Pivotal Studies coming
Summary and Conclusions

• Access to diabetes technology has exploded over the last 5 years
• Recent technological advances in diabetes have been a coordinated effort of traditional research and parent innovation
• Insulin pump therapy improves diabetes control in appropriate patients and is part of standard of care
• CGM improves control and prevents severe hypoglycemia in children and adults and is becoming standard of care
• Medtronic 670G is the first hybrid closed loop technology commercially available
  – May lower A1c, lead to more time in range with less variability AND hypoglycemia
• Many other close loop systems are in development and will likely see expedited FDA approval
Current State of Type 1 Diabetes
Updated T1D Exchange - 2015

K. Miller, Diabetes Care 38: 971