Current Status of Insulin Pump Therapy and Continuous Glucose Monitoring

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Disclosure Statement

- **Research and Grant Support to Employer:** Abbott, Biodel, DexCom, GSK, Halozyrne, Janssen, Lexicon, Lilly, MannKind, Medtronic, Novo Nordisk, Pfizer, Sanofi, Valeritas

- **Consultant:** Abbott, Halozyrne, Janssen, Medtronic, Novo Nordisk, Sanofi, Thermalin, Valeritas

- **Speaker’s Bureau:** Astra Zeneca, GSK, Janssen, Insulet, Lilly, Medtronic, Merck, Novo Nordisk, Sanofi, Valeritas, Vivus
DCCT Results
HbA1c and Relative Risk of Diabetic Complications

Relative Risk of Complications
Average US HbA1c Range 7.8-8.6%
AACE recommendation is 6.5%

Adapted from DCCT Research Group: NEJM 1993;329:977-986
The average type-1 patient has:

- Two symptomatic hypoglycemic events per week\(^1\)
- One or more episodes of severe, temporally disabling hypoglycemia per year
- Nocturnal hypoglycemia occurs ~ 8.5% of nights\(^2\)

The Type 1 Exchange, n=25,000 subjects, 67 sites\(^2\)
Hypoglycemia and Cardiovascular Events

- Tachycardia and high blood pressure
- Myocardial ischemia
  - Silent ischemia, angina, infarction
- Cardiac arrhythmias
  - Transiently prolonged corrected QT interval,
  - Increased QT dispersion
- Sudden death

Insulin Pump Use - Current

- Overall: 61%
- <6: 62%
- 6-12: 66%
- 13-17: 60%
- 18-25: 56%
- 26-49: 65%
- 50-64: 62%
- ≥65: 58%

The graph shows the percentage of insulin pump use across different age groups.
Insulin Pump Use Is Increasing

Overall: 58% Enrolled 9/1/2010 - 8/1/2012
6-12: 62% Current 4/1/2014 - 4/1/2015
13-17: 66%
18-25: 60%
26-49: 61%
50-64: 60%
≥65: 58%
Continuous Glucose Monitor Use

- Overall: 12%
- <6: 17%
- 6-12: 10%
- 13-17: 6%
- 18-25: 8%
- 26-49: 25%
- 50-64: 21%
- ≥65: 14%

Age (years)
CGM Use Is Increasing But Still Low

Enrolled 2010-2012 (8% use CGM overall)

Current 2014-2015 (12% use CGM overall)
CGM Use by Insulin Delivery Method

![Bar chart showing CGM use by age group and delivery method (Pump vs. Injection).]

- <6 years: 23% Pump, 6% Injection
- 6-12 years: 14% Pump, 2% Injection
- 13-17 years: 9% Pump, 1% Injection
- 18-25 years: 12% Pump, 3% Injection
- 26-49 years: 32% Pump, 11% Injection
- 50-64 years: 28% Pump, 10% Injection
- ≥65 years: 18% Pump, 9% Injection
Lower HbA1c in Insulin Pump Users
Lower HbA1c in CGM Users

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Non CGM Users</th>
<th>CGM Users</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;13</td>
<td>8.4%</td>
<td>7.8%</td>
</tr>
<tr>
<td>13-25</td>
<td>8.9%</td>
<td>8.1%</td>
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<tr>
<td>≥26</td>
<td>7.7%</td>
<td>7.3%</td>
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</table>
Lower HbA1c in CGM Users Regardless of Insulin Delivery Method

Mean HbA1c %

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Injection only</th>
<th>Pump only</th>
<th>Injection + CGM</th>
<th>Pump + CGM</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;13</td>
<td>8.7</td>
<td>8.3</td>
<td>7.9</td>
<td>7.8</td>
</tr>
<tr>
<td>13-&lt;26</td>
<td>9.3</td>
<td>8.6</td>
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<td>8.1</td>
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<tr>
<td>≥26</td>
<td>7.8</td>
<td>7.6</td>
<td>7.2</td>
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Lower HbA1c with Increased SMBG Frequency (excludes current CGM users)

<table>
<thead>
<tr>
<th>SMBG # Per Day</th>
<th>0-3</th>
<th>4-6</th>
<th>6-9</th>
<th>≥10</th>
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<tr>
<td>Age &lt;18</td>
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<tr>
<td>Pump</td>
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<tr>
<td>Injection</td>
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<td>Age ≥18</td>
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Current Pump Therapy Indications

- Need to normalize blood glucose (BG)
  - A1C > 6.5% or 7%
  - Glycemic excursions
- Hypoglycemia or Hypoglycemia unawareness
- Need for a flexible insulin regimen

Medicare requires: Fasting C-peptide to be $\leq 110\%$ lower limit of normal or $\leq 200\%$ lower limit of normal if CrCl $\leq 50$ ml/min with concurrent FPG $\leq 225$ mg/dL; or Beta Cell autoantibody positive (+ICA or +GAD antibodies)
The pump delivers basal and bolus insulin precisely and can be easily customized as needed to meet individual requirements.
CALCULATIONS FOR INSULIN PUMP DOSING

- Pump TDD
  - BASAL RATE: \( \frac{\text{PumpTDD} \times 0.5}{24\text{hr}} \)
  - CARB RATIO (CR): \( \frac{450}{\text{TDD}} \)
  - Sensitivity Factor (ISF)/ Correction: \( \frac{1700}{\text{Pump TDD}} \)

**Clinical Guidelines**
- Start with 1 basal rate, adjust according to glucose trends over 2-3 days
- Adjust to maintain stability in fasting state (between meals & during sleep)
- Add additional basals according to diurnal variations (dawn phenomena)
- Adjust based on lowfat meals with known carbohydrate content
- Acceptable 2-hr post-prandial rise is ~60mg/dL above pre-prandial BG
- Adjust carb. ratio in 10-20% increments based on post-prandial BG
- ALTERNATE METHODS
  - Carb Ratio: \((6 \times \text{Wt in kg/ TDD})\) or \((2.8 \times \text{wt in lbs/ TDD})\)
  - Fixed Meal Bolus = \(\frac{\text{TDD} \times 0.5}{3 \text{ equal meals}}\)
- Sensitivity Factor is correct if BG is within 30mg/dL of target range within 2 hours after correction
- Make adjustments in 10-20% increments if 2-hr post correction BGs are consistently above or below target.

**Clinical considerations on Pump TDD**
- Average values from Method 1 & 2
- Hypo patients -> start at lower value
- Hyper, elevated A1C or pregnant-> start at higher value
Factors Affecting A1C

- **Monitoring**
  - $A1C = 8.3 - (0.21 \times BG \text{ per day})$

*References*

- Bode et al. Diabetes Care 2002;25 439
Correlation between HbA$_1$c levels and number of SMBG measurements

Factors Affecting A1C

- Monitoring
  - A1C = 8.3 - (0.21 x BG per day)

- Recording 7.4 vs 7.8

- Diet practiced
  - CHO: 7.2
  - Fixed: 7.5
  - WAG: 8.0

Bode et al. Diabetes Care 2002;25 439
Monitor sends BG value to pump via radio waves:
No transcribing error

Enter carbohydrate intake into pump

Bolus calculator calculates suggested dose based on the ICR, CF, Target, and active insulin
Bolus Calculator: Example

Automatically calculates insulin bolus for the patient

Estimate Details
- Est total: 7.0 U
- Food intake: 60 gr
- BG: 200
- Food: 6.0 U
- Correction: 2.0 U
- Active ins: 1.0 U

ICR 1:10 gr

200 - 100 = 2.0 u
50 (SF)

Active insulin is subtracted from correction

ACT to proceed
ESC to back up
If on Smart Pumps and not at Goal

- Post meal BG too high
  - Lower CIR (Carb to Insulin Ratio)
- All BGs too high
  - Lower target and / or change CF (ISF)
- Fasting or pre meal BG too high
  - Increase basal
Case 1: Type 1 DM on pump at goal

- 28-year-old male with type 1 DM since age 17
- On pump since age 22
- No complaints; No assisted hypoglycemia
- A1C 6.7%
- Current insulin: 62 +/- 8 units/day (0.6 units/kg) with 59% basal; 41% Bolus
- SMBG 3.9/day; mean BG 155 +/- 118 mg/dL
## Device Settings Snapshot

**Tuesday 4/12/2011 13:19 PM**

### Basal
- **Maximum Basal Rate**: 2.00 U/hr
- **Temp Basal Type**: Percent of Basal

### Standard (active)
- **24-Hour Total**: 37.200 U

### Pattern A
- **24-Hour Total**: ...

### Pattern B
- **24-Hour Total**: ...

### Bolus
- **Maximum Bolus**: 25.0 U
- **Dual/Square (Variable)**: Off
- **Blood Glucose Reminder**: Off
- **Easy (Audio) Bolus**: Off
  - **Entry (Step)**: 0.10 U

### Sensor
- **Sensor**: Off
- **Transmitter ID**: ----
- **BG Units**: mg/dL

### Glucose Alerts
- **Off**
- **TIME**: 0.00, **Low (mg/dL)**: 80, **High (mg/dL)**: 240

### Carbohydrate Ratio (g/U)
- **TIME**: 0.00, **Ratio**: 8.0

### Insulin Sensitivity (mg/dL per U)
- **TIME**: 0.00, **Sensitivity**: 25

### Blood Glucose Target (mg/dL)
- **TIME**: 0.00, **Low**: 100, **High**: 100

### Notes

### Utilities
- **Alert Type**: Vibrate
- **Low Reservoir Warning**: Insulin Units
## Adherence (1 of 1)

### Glucose Measurements

<table>
<thead>
<tr>
<th></th>
<th>BG Readings</th>
<th>Sensor Duration (h:mm)</th>
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<tbody>
<tr>
<td><strong>Tuesday</strong>&lt;br&gt;3/29/2011</td>
<td>3</td>
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<tr>
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<td><strong>Thursday</strong>&lt;br&gt;3/31/2011</td>
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<tr>
<td><strong>Friday</strong>&lt;br&gt;4/1/2011</td>
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### Bolus Events

<table>
<thead>
<tr>
<th></th>
<th>Manual Boluses</th>
<th>Bolus Wizard Events</th>
<th>With Food</th>
<th>With Correction</th>
<th>Overridden</th>
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### Fill Events

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<tr>
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<th>Rewind</th>
<th>Cannula Fills</th>
<th>Cannula Amount (U)</th>
<th>Tubing Fills</th>
<th>Tubing Amount (U)</th>
<th>Suspend Duration (h:mm)</th>
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<td>0.7</td>
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</tbody>
</table>

### Summary

- BG Readings: 3.6/day 0m
- Sensor Duration: 0.0/day 0m
- Manual Boluses: 3.1/day 79.1%
- Bolus Wizard Events: 30.2%
- With Food: 11.6%

- Rewind: 4
- Cannula Fills: 0
- Cannula Amount (U): --
- Tubing Fills: 4
- Tubing Amount (U): 1.0 U/fill
- Suspend Duration: 3h 42m
### Diabetic Management Summary

<table>
<thead>
<tr>
<th>Reading Category</th>
<th>Count</th>
<th>Percentage</th>
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</thead>
<tbody>
<tr>
<td>Readings Below Target</td>
<td>17</td>
<td>33%</td>
</tr>
<tr>
<td>Sensor Avg (mg/dL)</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Avg AUC &gt; 140 (mg/dL)</td>
<td>--</td>
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</tr>
<tr>
<td>Avg AUC &lt; 70 (mg/dL)</td>
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<table>
<thead>
<tr>
<th>Nutritional and Insulin Summary</th>
<th></th>
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</thead>
<tbody>
<tr>
<td>Avg Daily Carbs (g)</td>
<td>175 ± 63</td>
<td></td>
</tr>
<tr>
<td>Carbs/Bolus Insulin (g/U)</td>
<td>6.8</td>
<td></td>
</tr>
<tr>
<td>Avg Total Daily Insulin (U)</td>
<td>62.3 ± 8.2</td>
<td></td>
</tr>
<tr>
<td>Avg Daily Basal (U)</td>
<td>36.8</td>
<td>59%</td>
</tr>
<tr>
<td>Avg Daily Bolus (U)</td>
<td>25.5</td>
<td>41%</td>
</tr>
</tbody>
</table>

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**Dinner: 4:00 PM - 10:00 PM**

- **Meals Analyzed:** 11
- **Avg Carbs:** 78g
- **Avg Insulin:** 10.4U
- **Avg Carbs/Insulin:** 7.5g/U

<table>
<thead>
<tr>
<th>3</th>
<th>5</th>
<th>5</th>
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<tbody>
<tr>
<td>188</td>
<td>151</td>
<td>161</td>
</tr>
</tbody>
</table>
WHAT PUMP TO CHOOSE: ???
Pump System Features in Common

- Several basal patterns
- Four year warranty
- 24-hour toll-free helpline
- Internal safety checks
- Child button lock-out
- Full Training Included
- Easy-programming
- Multiple infusion set options
- Extended bolus options
- Temporary basal options
- Programmable reminders
- Low battery warning
- Low insulin warning
- User-set active insulin time

Full Training Included
MiniMed® 530G with Enlite®
“Threshold Suspend”

- MiniMed 530G with Enlite
  - Senses a patient's glucose levels and stops delivering insulin when blood-sugar levels fall dangerously low
  - HCP sets level from 60-90 mg/dl

- Aspire trial showed a 32% reduction in nocturnal hypoglycemic events and a 38% reduction in mean area under the curve of nocturnal hypoglycemia events.
  - Notably, these benefits occurred without an increase in A1c levels.

- For patients 16 years or older

- Medtronic has applied for a new code with CMS for sensor-augmented pumps
Key Advantages

- Quick/simple bolus programming
- The reservoir: hold 300 units
- Small Basal Range: as low as 0.025 U/hr.
- Wireless Glucose Meter: Comes with Contour Next Link glucose
- Easily downloadable to online CareLink program for complete data analysis

Paradigm REAL-Time Revel and 530G System

Disadvantages

- Screen not color
- Not Water Proof: The pump is water resistant but not waterproof (do not drop this in the pool)
Medtronic Future

- Improved Sensor Performance
  - Enlite Enhanced; Enlite 3; Harmony Sensors
- Combined Sensor and Infusion set (DUO)
- 630G as their new waterproof pump for SAPT
- 640G for PLGS (Predictive Low Glucose Suspend)
- 670G for Hybrid Closed Loop

Not FDA approved
Animas OneTouch® Ping®
Animas: Animas Vibe®
**Key Advantages**

- **Display**: The color screen is self illuminating and easy to see.
- **Small Basal Range**: Insulin can be delivered to as low as 0.025 U/hr.
- **Maximum bolus**: 35 units
- **Water Proof**
- **Meter Remote**: One can deliver a bolus from the remote and have no need to access the pump when bolus.
- **Bolus calculator in both pump and meter remote**
- **Web-based download for complete data analysis**

**Possible Disadvantages**

- The reservoir is only 200 units
- Screen on meter gray-on-gray can be hard to see
- Require a few more button pushes to complete bolus calculation
- No back button, have to go back to main menu if ending up in the wrong place
Animas Future

- Artificial Pancreas Project with JDRF
- LifeScan Reveal Web-Based Software
- Calibre Bolus only pump
Accu-Chek Combo system

• Offers an easy, quick* & discreet way to manage insulin pump therapy

• “smart meter”

Intelligent communication in both directions using Bluetooth® technology
Key Advantages

- Display: Color screen on meter remote.
- The reservoir holds 315 units.
- With the Accu-Chek Combo system you get both the pump and meter. The system uses 2 way bluetooth communication. On the meter you can also access bolus advice, full color reports, reminders and it can also be used as a fully functioning pump. You can tuck away your pump all day and discreetly and easily access the pump screen on your meter.

Possible Disadvantages

- Bolus calculator only in meter remote – not in pump.
- Screen on pump gray-on-gray can be hard to see.
- Not Water Proof.
- Software not compatible for windows 7 or Mac.
ACCU-CHEK Aviva Expert
The first and only stand-alone meter with a built-in insulin calculator

Now patients can enjoy the meal without worrying about the math

• It simplifies the complex calculations needed by your carb-counting MDI patients to deliver precise insulin advice

• A survey of ACCU-CHEK Aviva Expert users:

  79% Reported increased confidence with insulin dose calculation\(^1\)

  52% Reported reduced fear of hypoglycemia\(^1\)

3 Simple Steps to Precise Bolus Advice

1. Test
2. Enter Carbs
3. Confirm Advice

- Test and receive blood sugar results
- Enter carb data and receive insulin dose advice
- Inject recommended dose and confirm on meter that advice has been followed
Future: ACCU-CHEK Insight Pump

Approved by EU; Not FDA approved
Future: ACCU-CHEK Insight Pump

Approved by EU; Not FDA approved
Tandem t:slim™ Insulin Delivery System

- Touch screen
- Durable light aluminum case
- Shatter-resistant glass
- Rechargeable battery
Key Advantages

- Display: Color touch screen – easy to see.
- Small Basal Range: A dosage can go as low as 0.001 u/hr starting at 0.1 units/hr. Lowest dosage increment on the market.
- Site change reminder can be set for 1, 2 or 3 days
- The reservoir: hold 300 or 480 units
- Water Proof
- The smallest insulin pump on the market
- Rechargeable: Fully charged lasts about 7 days.

Possible Disadvantages

- No glucose meter that transfers result to the pump.
- It’s recommended to periodically charge the pump 10-15 min/day
- Food bolus will only be reduced if BG is under 70.
- Take 9 min to change cartridge
- BG meter needs to be downloaded separately to get the BG log on combined report.
t:flex™ Insulin Pump

480 unit capacity to address the needs of insulin resistant patients
t:slim G4™ Insulin Pump
with Dexcom G4™ PLATINUM CGM
Infusion Sets

- Subcutaneous indwelling catheters
- Teflon cannula or steel needle
- Must be changed every 2-3 days (per insulin label)
Crimped soft canulae
Pump infusion sets: perpendicular vs oblique

Perpendicular (Sof-set™, Quick-set™, Ultraflex™)
- Easier insertion
- Prone to kink

Oblique (Silouette™, Tender™, Comfort™)
- More difficult insertion
- Less kinking

Sure T (metal Needle)
BD FlowSmart™ Insulin Infusion Sets
### BD FlowSmart™ Technology

**Product Profile**

<table>
<thead>
<tr>
<th>Design Features</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Compatible with Paradigm <em>and</em> Luer Lock connections</td>
</tr>
<tr>
<td>• Compatible with Medtronic insertion device</td>
</tr>
<tr>
<td>• Proprietary side-ported catheter</td>
</tr>
<tr>
<td>• 30G inserter needle and 28G catheter</td>
</tr>
<tr>
<td>• 10mm hub width and flexible base</td>
</tr>
<tr>
<td>• 8 different points of attachment of tubing to infusion hub</td>
</tr>
<tr>
<td>• Auto deployed needle shield</td>
</tr>
<tr>
<td>• Unit Package environmentally-friendly</td>
</tr>
</tbody>
</table>
Insulet OmniPod: Patch Pump platform

Just two simple parts

- **Fully integrated two-part design**
  - Built-in FreeStyle® BG meter that automatically incorporates BG levels into suggested bolus calculations and history records
  - Integrated infusion set, insulin reservoir, automated inserter, and batteries

- **Automated processes**
  - Cannula insertion
  - Priming

- **Intuitive user interface**
  - Full text navigation
  - Set-up wizard
  - Easy to teach, easy to learn

- **Waterproof Pod**
Key Advantages

- No Tubing
- Truly continuous insulin delivery: No need to disconnect for showering, swimming, other activities
- Small Size
- Auto insertion with the push of a button
- Built-in Blood Glucose Meter: You control the device with a handheld remote PDA with built-in Freestyle glucose meter.
- Lower Upfront Costs: The upfront costs for the device are less expensive. However, total cost may be higher over 4 years.
- Multiple infusion sites accessible

OmniPod manufactured by Insulet.

Possible Disadvantages

- The reservoir is only 200 units
- Forgetfulness: If you forget the PDA when you leave the house or work, you cannot adjust the insulin flow in the Pod. You will get your set basal.
- NOT covered by Medicare
- Minimum 85 unit fill
Future OmniPod

- Rechargeable PDA with mobile technology – i Phone like
- U-500 Regular Insulin and U-200 Humalog use in the OmniPod system
- Integrated CGM in Pod
- Developing the Artificial Pancreas with Harvard and DexCom
US Pump Usage: Total Patients Using Insulin Pumps thru 2006

Industry estimates
**Insulin Therapy Segmentation (US) – 2008**

>5.6 Million = 1.2 Million Type 1 (T1)
4.5 Million Type 2 (T2)

**Insulin Therapy:**

- **T1 Conventional** 368,160 (48%)
- **T1 MDI** 398,840 (52%)
- **T1 Pump Therapy** 361,000
- **T2 Pump Therapy** 37,000
- **T2 Conventional** 3,080,160 (69%)
- **T2 MDI** 1,383,840 (31%)

>31% Penetration in Type 1

<1% Penetration in Type 2

Source: Medtronic with 78% of the market
Type 2 Pump Study: OpT2mise Study

Objective

To compare the efficacy and safety of pump therapy (CSII) and multiple injection therapy (MDI) in patients with type 2 diabetes who had not responded to a basal-bolus regimen after active insulin titration.

Design

A 6-month randomized controlled trial, N=495 adults entered the run-in study phase. The MDI control group is crossing over to CSII at the end of the 6 month treatment period.

Subjects Characteristics

Subject eligibility criteria:
- **Run in phase:**
  - TD2 patient
  - A1C between 8.0% and 12%,
  - MDI users for at least 3 months with ≥3 injections/day (basal/bolus therapy)
  - Insulin requirements from 0.5 to 1.8 Units/kg/day
- **Randomization:**
  - A1C ≥ 8.0% and ≤12% despite insulin intensification
  - Insulin requirements from 0.7 to 1.8 Units/kg/day
  - Performing at least 2.5 SMBG tests per day during the run-in phase.

There were no significant differences between the groups at baseline except for HDL cholesterol (higher HDL-cholesterol concentration in the multiple injections group)
Primary End point: CSII Demonstrate a significant between Group A1c Reduction

Change in A1C - 6 months

Reduction of A1C:

CSII group : -1.1%
(A1C drop from 9.0% to 7.9%)

MDI group: -0.4%
(A1C drop from 9.0% to 8.6%)

A difference of 0.7% in favor of CSII group (p<0.001)

Insulin pump therapy (CSII) significantly improved glycemic control compared to multiple daily injections
Treatment Effect on Glucose Levels and Insulin Utilization

Baseline vs. 6-month blinded CGM data

<table>
<thead>
<tr>
<th></th>
<th>CSII</th>
<th>MDI</th>
<th>(CSII – MDI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Change in 24-h mean glucose level (mg/dL)</td>
<td>-23.0 ± (42.6)</td>
<td>-5.9 ± (30.2)</td>
<td>-17.1*</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>AUC change &gt;180 mg/dL (mg/dL × min)</td>
<td>-11.5 ± (25.5)</td>
<td>-2.2 ± (15.8)</td>
<td>-9.3*</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Change in time spent &gt;180 mg/dL (min / 24 h)</td>
<td>-225.6 ± (355.9)</td>
<td>-56.8 ± (256.3)</td>
<td>-168.7**</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>AUC change &lt;70 mg/dL (mg/dL × min)</td>
<td>0.0 ± (0.6)</td>
<td>-0.1 ± (0.9)</td>
<td>0.1</td>
<td>NS</td>
</tr>
<tr>
<td>Change in time spent &lt;70 mg/dL (min / 24 h)</td>
<td>8.8 ± (49.6)</td>
<td>5.1 ± (71.0)</td>
<td>3.7</td>
<td>NS</td>
</tr>
</tbody>
</table>

*, p<0.01; **, p<0.001

3 hours less time spent in Hyperglycemia per day

Subjects using the Insulin pump therapy (CSII) experienced greater reduction in mean glucose levels without notable increase in the time spent in hypoglycemia, while using less insulin vs. MDI

---

Insulin utilization

Subjects using the Insulin pump therapy (CSII) experienced greater reduction in mean glucose levels without notable increase in the time spent in hypoglycemia, while using less insulin vs. MDI
Simple Patch Pump for Type 2 DM: VGo

- Continuous preset basal insulin rate
  (20, 30 or 40 units/24 hrs)
- On-demand mealtime insulin via 2 unit clicks
  (Max 18 clicks/36 units)
- Uses only RAI
- Easy to fill, apply, use, and remove every 24 hours
- No electronics, batteries, infusion sets, or programming
- Fully disposable
V-Go® offers Simplicity and Physiologic Insulin Delivery
V-Go® Clinical Experience: HbA1c Reductions

<table>
<thead>
<tr>
<th>Cohort</th>
<th>Baseline</th>
<th>Change in HbA1c</th>
<th>3 Months</th>
</tr>
</thead>
<tbody>
<tr>
<td>SIMPLE</td>
<td>8.8%</td>
<td>-0.7</td>
<td></td>
</tr>
<tr>
<td>UMASS</td>
<td>10.7%</td>
<td>-2.4</td>
<td></td>
</tr>
<tr>
<td>UPP</td>
<td>8.8%</td>
<td>-1.2</td>
<td></td>
</tr>
<tr>
<td>EAP</td>
<td>9.3%</td>
<td>-1.9</td>
<td></td>
</tr>
</tbody>
</table>

N= 89- SIMPLE, 14- UMASS, 23- UPP, 16- EAP

2. Omer, A. et al. Poster presented at 73rd Scientific Sessions of the ADA; 2013 June 21-25; Chicago, IL. 980-P
V-Go® Clinical Experience:  
Change in Insulin

**SIMPLE**
All Cohorts  
Baseline 62 U  
TDD

**UMASS**
All Cohorts  
Baseline 119 U  
TDD

**UPP**
All Cohorts  
Baseline 56 U  
TDD

**EAP**
All Cohorts  
Basal Dose*

- N = 89- SIMPLE, 14- UMASS, 23- UPP, 16- EAP
- *Change in basal component of TDD only value available

2. Omer, A. et al. Poster presented at 73rd Scientific Sessions of the ADA; 2013 June 21-25; Chicago, IL. 980-P.
If A1C is Not to Goal

Must look at:

- SMBG frequency and recording
- Diet practiced
  - Do they know what they are eating?
  - Do they bolus for all food and snacks?
- Infusion site areas
  - Are they in areas of lipohypertrophy?
- Other factors:
  - Bolus % < 50% TDD
  - Fear of low BG
  - Overtreatment of low BG
Limitations of SMBG

Traditional glucose monitoring looks at only one point in time.

It doesn’t tell you where you’ve really been, or where you’re going.
C﻿GM Provides Patient with Live Bio-Feedback

What action should a patient take?

80 mg/dL
Seeing How Glucose is Trending

What action should be taken now?

80 mg/dL

- In 30 minutes, what might patient’s glucose be?
- What if patient is about to go to sleep or drive?

• 1 arrow indicates glucose has been changing 1 to 2 mg/dL/min
• 2 arrows indicate glucose has been changing >2 mg/dL/min.
CGM Provides Important Live Biofeedback

How might a patient react differently, to this?

Sensor data provides information that allows patients to make more informed decisions.

- 1 arrow indicates glucose has been changing 1 to 2 mg/dL/min.
- 2 arrows indicate glucose has been changing >2 mg/dL/min.
Continuous Monitoring Systems

CGMS® iPro™ Recorder

DexCom G4 and G5 Platinum

Paradigm or Guardian REAL-Time
Continuous Monitoring Systems

CGMS® iPro™ Recorder

Paradigm or Guardian REAL-Time

DexCom G5 Platinum
Dexcom G5
Mobile

G5
App

Dexcom Share/Follow
Abbott FreeStyle Libre Flash

14 day disposable CGM; No calibration needed

CE Marked only
Abbott FreeStyle Libre Flash

14 day disposable CGM; No calibration needed

CE Marked only
Abbott FreeStyle Libre Flash

14 day disposable CGM; No calibration needed

CE Marked only
CGM is effective for ALL... if you wear it.

Medtronic STAR 3 Sensor-Augmented Pump Trial

• The SAP group achieved a greater A1C reduction vs. MDI at 3 months and sustained it over 12 months

A1C Reduction for SAP and MDI Groups

Values are means ± SE. Comparisons between SAP group and MDI group are significant for each time period (P<0.001).
A1C Reduction Correlates to Increased Sensor Use

• The majority of patients used sensors ≥61% of the time
• Patients who used sensors ≥81% of the time reduced their mean A1C by 1.2% at 1 year vs. baseline

Values are the difference between the means ± SE. p=0.003 for association between sensor wear and A1C reduction at 1 year. Only 7 participants had sensor use of 20% or less, with a change in A1C of -0.43 at 1 year vs. baseline.
Sensor-Augmented Pumps Improve A1c without Increasing Hypoglycemia

- **DCCT (Adolescents & Adults)**
  - Severe Hypo Rate: 62.0 per 100 pt-yrs,
  - A1C: 9.0% → 7.2%

- **JDRF CGM (Adults, 1 Subject excluded)**
  - Severe Hypo Rate: 20.0 per 100 pt-yrs,
  - A1C: 7.6% → 7.1%

- **STAR 3 SAP (Pediatrics & Adults)**
  - Severe Hypo Rate: 13.3 per 100 pt-yrs,
  - A1C: 8.3% → 7.5%

Fundamentals of closed-loop systems

Subject Burden  Automation
Regulatory Ease  System Complexity
First Commercial Step in the Artificial Pancreas

- Threshold Suspend
Example of Threshold Suspend Cycle

Automatically suspends insulin delivery if sensor glucose reaches the user-set limit.

Insulin Suspends for 2 hours / Resumes for 4 hours

- Insulin infusion stops
- Suspend time maximum = 2 hrs
- Basal insulin infusion will resume even if glucose is below Thresh Suspend limit

Graph showing glucose levels over time:
- Basal Insulin
- 2 Hour Suspend
- 3 AM
- 6 AM
Threshold Suspend in CareLink® Professional

Daily Detail Report

Threshold Suspend  Manual Suspend
(Not represented in above report)
Threshold Suspend: Two Hour Suspension

- Patient did not respond to TS alarm
- Basal suspended for two hours, then automatically resumed
Threshold Suspend: Insulin Restarted

Patient:
- Cleared the alarm
- Tested BG
- Resumed insulin delivery immediately
Threshold Suspend: Insulin Restarted after One Hour

Patient:
- Cleared alarm and kept the basal rate suspended.
- Confirmed low with a fingerstick
- Resumed basal delivery after approximately one hour
## CareLink® Therapy Management Dashboard

### Pump Use

<table>
<thead>
<tr>
<th></th>
<th>Per Day</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Insulin TDD</strong></td>
<td>44.0 ± 4.2U</td>
</tr>
<tr>
<td><strong>Basal/Bolus Ratio</strong></td>
<td>42 / 58</td>
</tr>
<tr>
<td><strong>Manual Boluses</strong></td>
<td>0.0U (0.0 boluses)</td>
</tr>
<tr>
<td><strong>Bolus Wizard</strong></td>
<td>25.7U (4.6 boluses)</td>
</tr>
<tr>
<td><strong>Food</strong></td>
<td>23.8U (3.9 boluses)</td>
</tr>
<tr>
<td><strong>Correction</strong></td>
<td>4.3U (3.9 boluses)</td>
</tr>
<tr>
<td><strong>Override (+)</strong></td>
<td>0.2U (0.1 boluses)</td>
</tr>
<tr>
<td><strong>Override (-)</strong></td>
<td>-1.4U (0.3 boluses)</td>
</tr>
<tr>
<td><strong>Suspend Duration</strong></td>
<td>1h 22m per day</td>
</tr>
<tr>
<td><strong>Threshold Events</strong></td>
<td>2.3 per day</td>
</tr>
<tr>
<td><strong>Time</strong></td>
<td>1h 14m per day</td>
</tr>
<tr>
<td><strong>Res./Site Change</strong></td>
<td>Every 4.7 / 3.5 days</td>
</tr>
</tbody>
</table>

### Sensor Use

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Avg SG</strong></td>
<td>127 ± 45 mg/dL</td>
</tr>
<tr>
<td><strong>Wear Duration</strong></td>
<td>6d 20h per week</td>
</tr>
<tr>
<td><strong>Low SG Alarms</strong></td>
<td>20.5 per day</td>
</tr>
<tr>
<td><strong>High SG Alarms</strong></td>
<td>5.1 per day</td>
</tr>
</tbody>
</table>

**Only highest priority shown.**
Threshold Suspend: ASPIRE In-Home Study

Study conducted with Veo pump that is not FDA approved and not commercially available in the US. Study data and final report have not been submitted to FDA.


Mean AUC of Nocturnal Hypoglycemia Events

The severity and/or duration of nocturnal hypoglycemic events was lower in the Threshold Suspend Group.

37.5% reduction (p<0.001)
Hypoglycemic events were less frequent in the Threshold Suspend Group.

∆A1C was similar in the two groups. The 95% CI of the difference in ∆A1C (-0.05, 0.15) did not include the non-inferiority limit of 0.4%.

Study conducted with Veo pump that is not FDA approved and not commercially available in the US. Study data and final report have not been submitted to FDA.

Conclusions

• Insulin pumps provide basal and bolus therapy and are indicated for patients who are failing MDI in spite of frequent SMBG

• CGM use has been shown to improve glucose control with less risk of hypoglycemia

• Integrated Pump and CGM systems are available with future closed loop systems in development