Real World Experience
with the
Hybrid Closed Loop
Insulin Delivery System

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Disclosure to Participants
• Notice of Requirements For Successful Completion
  – Please refer to learning goals and objectives
  – Learners must attend the full activity and complete the evaluation in order to claim continuing education credit/hours
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  – Shannon Beasley, MSN, APRN, CPNP, CDE - No COI/Financial Relationship to disclose
  – Beth Olson: BAN, RN, CDE - No COI/Financial Relationship to disclose
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Learning Objectives
• Describe the impact of the 670G Hybrid Closed Loop system on safety and efficacy of glycemic parameters
• Explore the practical applications for implementation of the Hybrid Closed Loop system
• Address patient, caregivers’ and provider expectations of the 670G Hybrid Closed Loop system
Evolution of Pump Therapy

Insulin Pumps

- Accuchek Combo
- Animas One Touch Ping
- Medtronic 530G with Enlite CGM
- Tandem T-Slim
- Animas Vibe with DexCom
- Insulet Omnipod
- Medtronic 630G

Average Current HbA1c by Age

- 6yo
- 17yo
- 30yo

Average A1c

Age

T1D Exchange: Mean HbA1c by Insulin Delivery Method & CGM

- Pump only vs. Injection only: p<0.001*
- Pump + CGM vs. Pump only: p<0.001*
- P-values are adjusted by age and multiple comparisons.

Hybrid Closed Loop (HCL)

- Insulin pump software automatically increases or decreases insulin delivery based on sensor glucose values
- Patients are still required to enter carbohydrate information for dose delivery prior to eating ("hybrid")
- Success of HCL is dependent on insulin infusion site and sensor
- HCL works best on overnight/fasting glucose (possibly due to limits of current rapid acting insulins?)

Minimed 670G System

- FDA approved Sept 2016
- Initial patient use April 2017, full launch expected later in 2017
- Modes of function – Manual vs. Auto
MiniMed 670G Pivotal Trial

Methods:
- US (10 sites) and Israel
- 124 participants in total
  - 30 adolescents (age 14-20)
  - 94 adults (age 21-75)
- T1D for ≥ 2 years, A1c <10%, ≥ 6mos pump use
- Manual Mode for initial 2 weeks
- Auto Mode for 3mos with a 6 day/5 night hotel stay to monitor venous BG compared to sensor BG


Results:
- A1c changes
  - Baseline 7.4 ± 0.9%
  - End of study 6.9 ± 0.6%
- Sensor glucose
  - % in Target (71-180 mg/dL) 66.7% to 72.2%
  - % <50 mg/dL 1.1% to 0.6%
  - % <70 mg/dL 5.9% to 3.3%
  - % >180 mg/dL 27.4% to 24.5%
- Total daily dose of insulin
  - Baseline - 47.5 Units
  - End of study – 50.9 Units

Device Related Adverse Events

<table>
<thead>
<tr>
<th>Event</th>
<th>Run-in 2 wks.</th>
<th>Study 12 wks.</th>
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<tbody>
<tr>
<td>Total</td>
<td>8</td>
<td>21</td>
<td>36</td>
</tr>
<tr>
<td>Severe Hypoglycemia</td>
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<td>0</td>
<td>0</td>
</tr>
<tr>
<td>DKA</td>
<td>0</td>
<td>0</td>
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</tr>
<tr>
<td>Severe Hyperglycemia</td>
<td>*</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>Due to infusion set</td>
<td></td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>Due to software or hardware issues</td>
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<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Due to sensor issues</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Hypoglycemia</td>
<td>0</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>Skin irritation</td>
<td>3</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>Rash</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Pruritus</td>
<td></td>
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</table>

Dawn Phenomenon – Unpredictable

Programming for Dawn Phenomenon is ineffective and may be hazardous
- Almost every patient had Dawn phenomenon at some point
- Those with DAWN – had it 56% of the nights (median) rate

<table>
<thead>
<tr>
<th>Programmers</th>
<th>Non programmers</th>
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</thead>
<tbody>
<tr>
<td>Freq., Magnitude</td>
<td>Freq. Hypogly to Breakfast</td>
</tr>
<tr>
<td>42% nights, 54 mg/dL</td>
<td>37%</td>
</tr>
<tr>
<td>48% nights, 41 mg/dL</td>
<td>18%</td>
</tr>
</tbody>
</table>

Is this really a problem with SAP therapy today? Can closed loop therapy help address this problem?

M. Bouchonville, D. Schade et al
1200 ENDOCRINE PRACTICE NO 30/No. 12 December 2016
48 yo male with T1D 30 yrs
• Multiple basal rates
• a programmed increase from 1-3 AM (0.9-2.0 u/hr)

Conclusion:
Alternate basal rate overnight needs to be increased

Overnight glucose control - Hyperglycemic

48 yo male with T1D 30 yrs
• Multiple basal rates
• a programmed increase from 1-3 AM (0.9-2.0 u/hr)

Conclusion:
Alternate basal rate overnight needs to be decreased

Overnight glucose control - Hypoglycemic

48 yo male with T1D 30 yrs
First week closed loop.
Overnight basal delivery of insulin:
Very low from 2-4 AM

Second week closed loop
Overnight glucose control
Good

Overnight basal insulin:
Very low (Zero) from MN 2AM then down 3-4 AM, up 5-6AM

Case 1: Overnight Open Loop - glucose variable insulin fixed
(attempt at personalized rate)

Closed Loop - glucose tight insulin variable (basal insulin rates change every hr. every day)

Overnight insulin variable
**Manual Mode**

**Pre-Auto Mode:**
- Normal smart pump functionality

**Post-Auto Mode Start:**
- Will go into Manual Mode when Safe basal is >90 minutes without resolution
- Or will leave Auto Mode and go directly to Manual Mode if…
  - High sensor glucose: >300 mg/dL x 1 hour or >250 mg/dL x 3 hours
  - Insulin flow blocked

**Manual Mode Screens**

- Without CGM
- With CGM
- Suspend Before Low or Suspend on Low

**Starting Auto Mode**

- After 48 hours wearing pump (even without CGM), Auto Mode is available
- CGM is necessary to activate Auto Mode when ready
- Turn off “Suspend on Low/Threshold” manually
- If Auto Mode does not start, the insulin pump will prompt into a troubleshooting screen

**Checking for Auto Mode Readiness**

- Auto Mode Readiness
  - No requirements
  - Auto Mode turned off
  - Sensor not ready
  - Data in progress
  - Delivery suspended
  - Carb ratio not set
  - Temp basal rate
  - Active insulin updating
  - Auto Mode warming up

- Auto Mode Readiness
  - OK for Auto Mode
  - Auto Mode turned on
  - Sensor not ready
  - Data in progress
  - Delivery OK
  - Carb ratio not set
  - Temp basal rate
  - Active insulin updating
  - Auto Mode warming up

**670G HCL Components**
### Auto Mode Ready

![Auto Mode Readiness](image)

- **We're Good to Go!**

### Auto Mode – At a Glance

#### Auto Basal Delivery

#### Safe Basal

- Fixed rate by algorithm, based on last 6 days of data
- Can last up to 90 min, then either back to Auto or Manual
- Safe basal is activated in the following situations:
  - After sensor change during warm-up
  - No sensor glucose or calibration expired
  - Sensor reading lower than SMBG
  - Sensor glucose and SMBG are >35% apart
  - Maximum basal rate for 4 hours
  - Minimum rate (or no insulin) for 2.5 hours

### What to Know About Auto Mode

- Goal is to stay in Auto Mode most of the time (eg >80%)
- Start Auto Mode early in the day so not calibrating at night
- If exiting out of Auto Mode: Remember to turn “Suspend on Low” ON
- If patient takes an insulin injection (pensyringe), Auto Mode will not factor it in as insulin on board nor with correction recommendations
- There are no square/dual wave boluses in Auto Mode
- Can have Quick Delivery (15 units/min) vs Regular Bolus (1.5 units/min)

### Auto Mode Screens

- **Auto Basal Delivery**
- **Safe Basal Delivery**
- **Temp Target**

### Safe Basal

- **Temp Target**
  - Temporary setting to keep glucose around 150 mg/dL
  - Consider use with exercise/activity
  - Other unique situations?
What is Needed to Initiate Hybrid Closed Loop Systems in Your Clinic?

Differentiating the Parts

<table>
<thead>
<tr>
<th>Minimed 530G</th>
<th>Minimed 630G</th>
<th>Minimed 670G</th>
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<tbody>
<tr>
<td><strong>Meter</strong></td>
<td>Contour Next Link</td>
<td>Contour Next Link 2.4</td>
</tr>
<tr>
<td><strong>Transmitter</strong></td>
<td>MiniLink Transmitter (MMT-7703)</td>
<td>Guardian Link Transmitter (MMT-7763)</td>
</tr>
<tr>
<td><strong>Sensor</strong></td>
<td>Enlite Sensor (MMT-7008) 6-day wear</td>
<td>Enlite Sensor (MMT-7008) 6-day wear</td>
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<tr>
<td><strong>Carelink USB</strong></td>
<td>Carelink USB (MMT-7306)</td>
<td>Carelink USB (MMT-7306)</td>
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<tr>
<td><strong>FDA Approved</strong></td>
<td>≥16 years old</td>
<td>≥16 years old</td>
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External Differences

<table>
<thead>
<tr>
<th>Minimed 630G</th>
<th>Minimed 670G</th>
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<tbody>
<tr>
<td><strong>Sensor</strong></td>
<td>Guardian Sensor (3) (MMT-7020) 7-day wear</td>
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<tr>
<td><strong>Carelink USB</strong></td>
<td>Carelink USB (MMT-7306)</td>
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<tr>
<td><strong>FDA Approved</strong></td>
<td>≥14 years old</td>
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Standard Menu Icons

<table>
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<tr>
<th>ICON</th>
<th>Meaning</th>
<th>Other</th>
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<tbody>
<tr>
<td>☀️</td>
<td>Battery</td>
<td>☀️</td>
</tr>
<tr>
<td>🍴</td>
<td>Reservoir</td>
<td>🍴</td>
</tr>
<tr>
<td>🎧</td>
<td>Audio</td>
<td>🎧</td>
</tr>
<tr>
<td>🔍</td>
<td>Connection</td>
<td>🔍</td>
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<tr>
<td>🔐</td>
<td>Calibration</td>
<td>🔐</td>
</tr>
<tr>
<td>🔥</td>
<td>Auto Mode Readiness</td>
<td>🔥</td>
</tr>
</tbody>
</table>

Expectations of Closed Loop Systems

- “Artificial Pancreas” vs. “Hybrid Closed Loop System”
- Perception of HCL in those already using technology differs from those who are not
- Overuse/ misuse of CGM has been associated with unrealistic expectations
- More understanding is needed as more systems become available
General Considerations for Starting HCL

- Similar selection criteria for current pump use
  - Ability to respond to alarms and troubleshoot pump/CGM
  - Knowledge of carb counting and bolusing before eating
  - Willingness to learn a new system and ability to transition smoothly
- Prior pump/CGM use is encouraged, though is not thought to be mandatory
- There is no "share" feature with parents/family (yet)

HCL Timeline for Experienced Pumper

- Step 1 (Intro) → 2-3 weeks
- Step 2 (Insurance) → 1 week
- Step 3 (Training) → 1-2 weeks
- Step 4 (Auto-Mode) → 1-2 weeks
- Step 5 (Fine Tune) → 1 week
- Step 6 (Follow-up) → 3-4 weeks

2-3 Months In Total

Potential Billing for Experienced Pumper

- Step 1: CDE - 30 minutes (Billing Code G0108)
- Step 4: MD/NP/PA - 30 minutes (Billing Code 99214)
- Step 5: MD/NP/PA - 30 minutes (Billing Code 99213, Sensor Interpretation 95251)
- Step 6: CDE - 30 minutes (Billing Code G0108), MD/NP/PA - 30 minutes (Billing Code 99214)

Layers of Diabetes Demands

Device Management

Accuracy of carb counting

Exercise

Timing of insulin doses

Healthy eating habits

Changing Layers of Demands

Device Management

Accuracy of carb counting

Exercise

Timing of insulin doses

Healthy eating habits

Additional Considerations

- Continued management burden (just as many, if not more, BG checks)
- Areas for device placement ("real estate")
- Insulin action times
- Device cost
- Medication cost
- Insurance limitations
- How will healthcare providers get training, adopt, and get reimbursed
Calibration

**Things to Know:**
- Consider sensor start time
- Sensor warm-up = 40 min to 2 hours
- Minimum of 2x/day; Ideally 3-4x/day
- Watch arrow trends
- Follow pump requests

Don't Be Late, Calibrate!

Clinical Pearls

- Will need physician, educator, and patient education
- Corrections likely are slower (for safety), maybe bolus earlier
- If BG is >150, will suggest a correction
  - Cannot adjust the recommendation, only accept or decline
- No square/dual wave in auto mode
- Active insulin time in the pivotal trial was 3 hours (most patients needed lower than their previous settings)
- Might be ideal for dawn phenomenon
- New way of thinking about pump (eg 50:50 rule may not apply)

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Basal to Bolus Ratios

- The "50/50 Rule" may not work for HCL
  - Other "Rules" like 500 or 1800 may also be incorrect

- For example, in 1 HCL trial:
  - Before Closed Loop: 71% basal
  - In Closed Loop: 71% bolus

- Maybe "Rule of 30/70" is more appropriate?

Alerts & Alarms

**Possible Reasons:**
- Calibration required
- Alert min or max reached or approaching these levels
- Delivery suspension
- Safe basal engaged
- Auto mode exit
- Blockage

Steering Clear of Hypoglycemia

- Avoid acetaminophen to maintain sensor glucose accuracy
- Activate temp target an hour before planned exercise
- Less CHO needed to treat mild lows
- If in manual mode, patient must actively turn on suspend before low feature
- Watch sensor glucose trends
- Respond to low glucose alarms

Post-Study Perceived HCL Benefits

- Steady glucose levels
- Overnight Benefit
- Mealtime Benefit
- Fewer long-term complications
- Better quality of life
- Mental relief
- A break from diabetes

"I mean typically I don't eat a burger and pizza for dinner... but I was like, "No, why not? Let's see how the system can handle it," and I was pleasantly surprised."
Post-Study Limitations

- Unexpected tasks
- Hard to wear
- Not responsive enough to highs given what I can achieve on my own
- Being reminded of diabetes

“I checked way, way more than I normally do at home.”

“I think I still thought about everything just as much or more. It didn’t really take away from the diabetes burden.”

Iturralde et al, Diab Educator, 2017

Case Study - Hyperglycemia Day 1

2:40pm BG 115mg/dl, bolus 10.8 units; 86 gm carb

Rapid rise in SG-gives correction insulin via syringe; changes infusion set, sensor. Notes site is wet with insulin. Gives another bolus via pump.

Hyperglycemia Day 2

12am-Hypo and sensor issues

6am-BG>300, ketones 2.3mmol/L. Gives correction bolus via pump and calls MD. New insulin bottle, correction insulin via syringe, change infusion site, increase fluids

Infusion catheter was kinked!

Hyperglycemia Resolved

Words to the Wise

- Expect post-meal rise
- Respond to alerts and alarms
- Enter BG values for meals and correction boluses
- Target sensor glucose of 120 mg/dL means “gentle landing” in lieu of aggressive correction
- Check the display screen frequently, especially at bedtime
- Work to stay in auto mode and the system will work for you!

Carelink Reports
Step 1: Assess glucose profile and evaluate for hypoglycemia, hyperglycemia and variability.


Step 3: Review statistics panel.

Step 4: Assess Auto Mode exits (see Step 5).

Step 5: Review Exit Reason Details and time periods.

Step 6: Review bolus patterns and AIT sails.

Step 7: Review Auto-Basal and Basal rates.

Step 8: Note time change, temp targets, etc.

Carelink Reports – Pump Settings

Conclusions:
- Technology in T1D has come a long way.
- Research data with HCL is encouraging.
- As the first HCL system is commercialized with a broader patient population included – outcomes will be important:
  - Glucose control
  - Quality of life, reduced burden
  - Cost / reimbursement
- Training of professional & patients will be critical.

Any Questions?