Continuous Glucose Monitors for Diabetes Management

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Objectives

• What is Continuous Glucose Monitor
  • Technology, Accuracy, Tolerability, Types of devices
• What’s available today?
• Is CGM effective?
• Society Recommendations
• Clinical Use & indication
• Financial benefit
• Future
• Cases/Questions
• Conclusion
Background

- Diabetes is a multisystem disease which may often lead to many serious complications
- Impacts 30 million lives in the United States (37)
- 30% of all patients with diabetes are treated by insulin (38)
- Adult glucose monitor adherence rates
  - 44% in adults with T1DM
  - 24% for adults with T2DM.
~6 Million People with Diabetes on Intensive Insulin Therapy

Current CGM patients
What is CGM?

- Continuous Glucose Monitor
  - Available since 1999 Medtronic (45)
- Various challenges in the past
  - Bulky design
  - Lack of accuracy
  - Lacking FDA approval for therapy augmentation
  - Inconvenient, Multiple calibration, fingersticks
  - Complicated data output
  - Lack of familiarity by the clinicians (7).
What is CGM?

• General Concept
• Two major components
  • Sensor + transmitter component
    • Attached to the patient
    • Small and light weight
    • Filament inserted to the subcutaneous tissue
    • Sending signal to reader
  • Reader/receiver component
    • Interprets the signal into data and store data
What is CGM?

- Technological Concept (47)
What is CGM?

- How is glucose measured?
  - Glucose oxidase enzymatic reaction
    - Oxygen as the cofactor to carry electron from glucose molecules
    - Concentration based electric current generated
    - Electrical current signals are used by the reader to generate data
Accuracy

• **MARD - Mean Absolute Relative Difference**

• **MARD** is the result of a mathematical calculation that measures the average disparity between the sensor and the reference measurement. The lower the MARD, the more accurate the device is considered.

• **Calculate MARD**
  - Difference of Capillary BG (blood glucose) vs Difference CGM BG
  - Average of $|\text{Difference}| / \text{mean of cap. BG} \times 100\%$

• **Where we are at today?**
  - 10% of MARD
Accuracy

Dexcom System MARD* by Generation

Accuracy (MARD) %

26%
17%
16%
13%
9%

STS 3-Day (2006)
SEVEN (2007)
SEVEN Plus (2008)
G4 PLATINUM (2012)
G5 Mobile (2015)

G6 No Cal (Pre-Pivotal)
Device Types

- **Professional type**
  - Masked data - patient is unable to see real-time measurement
  - Pros
    - Simplicity
    - Stick and follow up
    - Relatively cheaper and more available
    - Understanding glucose excursion and detecting unusual trends
  - Cons
    - Unable to provide real-time data
    - No alarm
    - Unable to provide sense of empowerment
Device Types

• Personal type
  • Real-time data available on personal reader device via a scanner or even smartphones or smart watches
  • Pros
    • Replacing traditional capillary glucose measurement, no fingersticks
    • Lifestyle modification
    • Alarm for lows
    • Understanding the disease
  • Cons
    • Overwhelmed by result
    • Expensive
Current Models

- Dexcom
  - G6 approved 3/2018
  - G5
- Abbott FreeStyle Libre
  - Pro
  - Personal (available since 1/2018)
- Medtronic
  - MiniMed 670 with Guardian Sensor 3
  - MiniMed 630 with Enlite Sensor
Dexcom

- **Devices**
  - Dexcom G5 and G6

- **Duration:**
  - 7 days for G5
  - 10 Days for G6

- **Accuracy (MARD %)**
  - MARD = 9%

- **Calibration**
  - G5 2x/day
  - G6 none, but capable

- **Dexcom G5 is first approved to augment treatment without fingerstick confirmation**
Dexcom

- **Dexcom G6**
  - Newest model approved 3/2018
  - MARD : 9%
  - Calibrations: None
  - Minimized acetaminophen affect on sensor
FreeStyle Libre

- Devices
  - FreeStyle Libre
  - FreeStyle Libre Pro
- Duration:
  - Personal: 10 days
  - Professional: 14 days
- Calibration: none
- Accuracy (MARD %)
  - Personal = 9.7
  - Professional = 12.3
Medtronic Minimed

- MiniMed 670 with Guardian Sensor 3
  - Duration
    - 14 days
  - Calibration
    - Every 12 hours
    - Can calibrate up to 3-4 times/day
  - Accuracy (MARD)
    - 9.64-10.55%
    - Accuracy improves with 3-4 calibrations/day
Medtronic Minimed

- MiniMed 630 with Enlite Sensor
  - Duration
    - 14 days
  - Calibration
    - Every 12 hours
  - Accuracy (MARD)
    - 11.05%
How do they compare to fingerstick?

- Decrease time spent in hypoglycemia or hyperglycemia
Is It Effective?

- A1C reduction
  - T1D
  - T2D
- Reduce time spent in hypoglycemia
- Increase time spent in target range
- Facilitate lifestyle modification
- Improve Quality of life
Is It Effective?

• A1c Reduction in T1D
  • 2008 JDRF Trial
    • Reduce A1C by 0.53%-0.8% without increasing the frequency of hypoglycemia, more effective on 25 or older
  • A1C Reduction by 1.0% without intensify insulin therapy (48)
  • The DIAMOND Randomized Clinical Trial
    • A1C reduction by 1.3% in patients with starting A1C of 8.5% (47)
Clinical Trials

- DlaMondD Type 1 study (2016)
  - A1C reduction
  - Reduction of time in hypoglycemia or hyperglycemia

Clinical Trials

- **GOLD randomized clinical trial (2017)**
  - Shows improvements in quality of life
  - 0.43% A1c reduction in CGM group
  - 80% decrease in severe hypoglycemia

Is It Effective?

• A1C Reduction in T2D
  • type 2 DM improvement with reduce calories intake, better a1c reduction (51: Yoo et al. 2008)
    • A1C reduction of 0.7
  
• More hypoglycemia detection with CGM group
  • CGM 56.9% vs SBMG 26.4%
    • (52: Zick et al 2007)
Clinical Trials

- COMISAIR study (2016)- CGM drives A1c reduction
Is It Effective?

- Lifestyle Modification
- Increase frequency of glucose check
  - check increase efficacy
- Help reduce burnout and improve quality of life for T2D (Fonda et al 2016:49)
- CGMS feedback for individuals with type 2 diabetes may improve physical activity levels and reduce risk factors for diabetes-related complications
  - (Allen et al 2008:50)
Is It Effective?

• Hypoglycemia Duration Reduction
  • By 79% overall by Diamond Trial 2017
  • 38% (T1D), Impact trial 2016
  • 43% (T2D), Replace Trial 2017

• More hypoglycemia detection
  • 72 hr period
  • CGM 56.9% vs SBMG 26.4%

• Nocturnal hypoglycemia reduction
  • 83 patients (65-80 yo), 39% with nocturnal hypoglycemia
    • Klimontov and Myakina in 2017
Is It Effective?

• Increase time spent in target range
  • By 1.2 hour
  • By 38-43% overall
    • DIAMOND Randomized Clinical Trial (Beck 2017)
Should I use it?

- AACE Recommendations

<table>
<thead>
<tr>
<th>American Association of Clinical Endocrinologists (AACE) and American College of Endocrinology</th>
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<tbody>
<tr>
<td><strong>2010 Recommendations</strong>^1</td>
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<tr>
<td>Adults</td>
</tr>
<tr>
<td>Type 1 with hypoglycemic unawareness or frequent hypoglycemia; A1C over target</td>
</tr>
<tr>
<td>Type 2 should only utilize professional CGM systems to evaluate treatment plan and patient's glucose control</td>
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<thead>
<tr>
<th><strong>2016 Recommendations</strong>^2</th>
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<tbody>
<tr>
<td>Adults</td>
</tr>
<tr>
<td>All patients with Type 1, especially those with severe hypoglycemia and hypoglycemia unawareness</td>
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<tr>
<td>All Type 2 patients who take multiple insulin injections, basal insulin or sulfonylureas and who are at risk for hyperglycemia, hypoglycemia or hypoglycemia unawareness</td>
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<table>
<thead>
<tr>
<th>Pediatrics</th>
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<tbody>
<tr>
<td>Type 1 who have achieved A1C levels of &lt;7% or those &gt;7% who can wear the CGM daily</td>
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<table>
<thead>
<tr>
<th>Conclusions</th>
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<tr>
<td>More research should be performed to determine which patients are the best candidates for CGM.</td>
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<tbody>
<tr>
<td>Conclusions</td>
</tr>
<tr>
<td>CGM usage has <strong>improved clinical diabetes outcomes</strong> by reducing hypoglycemia.</td>
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<tr>
<td>CGM should be used in <strong>all patients</strong> who have severe hypoglycemia or hypoglycemia unawareness.</td>
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<tr>
<td>Consensus of experts call for <strong>wider use of CGM</strong> and emphasizes the need for additional studies that can address efficacy and cost.</td>
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Should I use it?

- ADA Recommendations

<table>
<thead>
<tr>
<th>American Diabetes Association</th>
<th>2007-2013 Recommendations³</th>
<th>2016 Recommendations⁴</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Adults</strong></td>
<td>Patients with A1C &lt;7% and useful in those with hypoglycemia unawareness or frequent hypoglycemic episodes.</td>
<td>Patients with Type 1 diabetes and those with hypoglycemia unawareness or frequent hypoglycemic episodes.</td>
</tr>
<tr>
<td><strong>Adults (ages 65+)</strong></td>
<td>N/A</td>
<td>Patients who have been successfully using CGM should continue to have access after age 65.</td>
</tr>
<tr>
<td><strong>Pediatrics</strong></td>
<td>Reduces glycemic excursions, if used correctly.</td>
<td>Reduces glycemic excursions and has shown to reduce missed school days with &gt;70% usage.</td>
</tr>
<tr>
<td><strong>Conclusions</strong></td>
<td>CGM is an evolving technology and a potential tool in lowering A1C.</td>
<td>CGM used in conjunction with intensive insulin therapy is a <strong>useful tool to lower A1C in adults</strong> (ages ≥25 years) with Type 1 diabetes and can be <strong>helpful in lowering A1C in children, teens and younger adults</strong>.</td>
</tr>
</tbody>
</table>
Should I use it?

- ADA 2018

**Recommendations**
- Most patients using intensive insulin regimens (multiple-dose insulin or insulin pump therapy) should perform self-monitoring of blood glucose (SMBG) prior to meals and snacks, at bedtime, occasionally postprandially, prior to exercise, when they suspect low blood glucose, after treating low blood glucose until they are normoglycemic, and prior to critical tasks such as driving. B
- When prescribed as part of a broad educational program, SMBG may help to guide treatment decisions and/or self-management for patients taking less frequent insulin injections B or noninsulin therapies. E
- When prescribing SMBG, ensure that patients receive ongoing instruction and regular evaluation of SMBG technique, SMBG results, and their ability to use SMBG data to adjust therapy. E
- When used properly, continuous glucose monitoring (CGM) in conjunction with intensive insulin regimens is a useful tool to lower A1C in adults with type 1 diabetes who are not meeting glycemic targets. A
- CGM may be a useful tool in those with hypoglycemia unawareness and/or frequent hypoglycemic episodes. C
- Given the variable adherence to CGM, assess individual readiness for continuing CGM use prior to prescribing. E

- When prescribing CGM, robust diabetes education, training, and support are required for optimal CGM implementation and ongoing use. E
- People who have been successfully using CGM should have continued access after they turn 65 years of age. E
Ways to use

- T1D and T2D with hyper or hypoglycemia
- Insulin pump integration
- Hypoglycemia unawareness
- Poor glycemic control either on insulin or not
- Motivated patient seeking further managing glycemic control
- Dawn phenomenon
- Nocturnal hypoglycemia
- Somogyi effect
- Post-prandial control vs Preprandial control
- Pregnant patients
# Glucose Statistics

**Average Glucose (mmol/L):** 9.3

**Estimated HbA1c:** 7.5%

<table>
<thead>
<tr>
<th>Glucose Exposure</th>
<th>Glucose Ranges</th>
</tr>
</thead>
<tbody>
<tr>
<td>4.9 - 8.4*</td>
<td>&lt; 3 mmol/L</td>
</tr>
<tr>
<td>4 - 6*</td>
<td>&lt; 3.3 mmol/L</td>
</tr>
<tr>
<td>0*</td>
<td>&lt; 4*</td>
</tr>
<tr>
<td>&lt; 6*</td>
<td>&gt; 3.9 - 10 mmol/L</td>
</tr>
<tr>
<td>0*</td>
<td>&gt; 10 mmol/L</td>
</tr>
<tr>
<td>0*</td>
<td>&gt; 13.9 mmol/L</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Coefficient of Variation</th>
<th>SD (mmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>43.6%</td>
<td>4.1</td>
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</table>

<table>
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<tr>
<th>% Time CGM Active</th>
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<tbody>
<tr>
<td>76.0%</td>
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</table>

*Reference ranges calculated from a population without diabetes. Glucose Range reference values based on a target range of 3.9 - 10.0 mmol/L.*

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**Graph:**

- Curves/points represent glucose frequency distributions by time regardless of data.

- **50%** represents the median glucose levels.

- **25/75% - IQR** indicates the interquartile range.

- **10/90%** shows the range of glucose levels.

- **Target Range** is highlighted in the graph.
Pattern Snapshot for Patient Example
Mar 3 - Mar 8, 2017
(6 days)

Avg SG: 149 mg/dL
Estimated A1C (1): 6.8% calculated from SG values

Time in range: 58% Above 140 mg/dL
35% in target range
7% Below 70 mg/dL

OBSERVED PATTERNS & SOME POSSIBLE CAUSES (2)

1. Variable SG - Overnight
   11:00 PM - 6:00 AM
   Glucose variability during overnight for 6 days
   - Erratic food intake day before?
   - Erratic exercise schedule day before?
   - Erratic sleep pattern?
   - Oral medication(s) day before omitted or incorrectly timed?
   - Basal insulin injection missed?
   - Pre-meal insulin in prior evening(s) incorrectly timed or omitted?

2. Variable SG - Post-breakfast
   6:00 AM - 10:00 AM
   Glucose variability during post-breakfast for 6 days
   - Variable food intake?
   - Oral medication(s) too high or incorrectly timed?
   - Pre-breakfast insulin incorrectly timed, too low, too high, or omitted?
   - Insulin to carbohydrate ratio not optimal for pre-meal insulin?

3. Low SG - Pre-breakfast
   6:00 AM - 10:00 AM
   3 out of 6 days excursions observed:
   - 3 day(s) 50 - 70 mg/dL
   - 0 day(s) < 50 mg/dL
   - Less food intake in prior evening(s)?
   - Breakfast delayed?
   - More exercise in prior evening(s)?
   - Oral medication(s) too high or incorrectly timed?
   - Basal insulin injection in evening(s) too high?
   - Alcohol consumed in prior evening(s)?

---

(1) Estimated A1C does not replace Lab measurement and is calculated from limited SG data.
(2) Suggested considerations are limited and do not replace the opinion or advice of the healthcare provider. Please see User Guide on how patterns and possible causes are identified.
Daily Patterns (with Ambulatory Glucose Profile)
September 7, 2015 – September 20, 2015 (14 days)

Estimated A1c 7.8%, or 62 mmol/mol

Estimated A1c is an estimated value and does not replace the lab HbA1c blood test.
For illustrative purpose only. Not actual patient data.
Financial and Practicality

• Simplicity
• CPT reimbursement $ for fees data
• 95249 ($56.16)
  • Ambulatory CGM of interstitial tissue fluid via a subcutaneous sensor for a minimum of 72 hours; patient provided equipment, sensor placement, hook-up, calibration of monitor, patient training, removal of sensor, and printout of recording.
• 95250 ($156.60)
  • Ambulatory CGM of interstitial tissue fluid via a subcutaneous sensor for a minimum of 72 hours; physician or other qualified health care professional (office) provided equipment, sensor placement, hook-up, calibration of monitor, patient training, removal of sensor, and printout of recording.
• 95251 ($36.72)
  • Ambulatory CGM of interstitial tissue fluid via a subcutaneous sensor for a minimum of 72 hours; analysis, interpretation and report.
Future development

- Eversense by Senseonics
- 90-day implant
- MARD of 11.6%
Case 1

- 32 year-old male with Type 1 diabetes for 12 years
  - A1C 7.8%
  - ICR of 1 unit:15 grams CHO, CF of 1 unit:50mg/dL
  - Tests with fingerstick blood glucose checks 4-6 times daily
Case 1

Jake with CGM

- 10:45 AM: CGM ALARM, 200 mg/dL, Exercised 30 min
- 9:32 AM: 138 mg/dL, Dosed 4 units with breakfast
- 11:15 AM: 150 mg/dL, Ate lunch
- 2:05 PM: 112 mg/dL, Dosed 6 units, Snack
- 5:15 PM: 160 mg/dL, Snack
- 8:30 PM: CGM ALARM, 200 mg/dL, Dosed 1 unit
- 9:20 PM: Checked BG, 175 mg/dL, Dosed 8 units for dinner with wine
- 11:25 PM: 100 mg/dL, Snacks for correction

Icons:
- Did Not Test to Event
- SMBG
- CGM Readings
- CGM Alerts
Case 2

- 47-year-old female with Type 2 diabetes
- A1c 9.2%
- 4 units at breakfast, 5 units at lunch and dinner
- Has missed morning doses of insulin due to fears of low blood glucose in the morning
- Tests fingerstick blood glucose 1-2 times daily
Case 2

Mary without CGM

- 6:45 AM: 140 mg/dL SMBG
- 7:15 AM: Ate oatmeal, skipped breakfast dose
- 12:35 PM: Dosed 5 units
- 3:05 PM: Snack, ate cookie
- 6:30 PM: Dosed 5 units with dinner
- 10:00 PM: 175 mg/dL SMBG

Did Not Test to Event

SMBG
Case 2

Mary with CGM

- **8:32 AM**
  - HIGH ALERT
  - 200 mg/dL
  - Won’t skip breakfast dose tomorrow. Took stairs and walked for 15 min.

- **7:15 AM**
  - Ate oatmeal
  - Skipped breakfast dose

- **6:45 AM**
  - 140 mg/dL
  - SMBG

- **12:35 PM**
  - 211 mg/dL
  - No arrow but BG high
  - Ate lunch but removed 1 slice of bread
  - Took lunch insulin

- **3:05 PM**
  - 165 mg/dL
  - Glucose steady
  - Ate 1/2 cookie

- **6:30 PM**
  - 117 mg/dL
  - Glucose steady
  - Ate dinner
  - Dosed 5 units insulin

- **10:00 PM**
  - 150 mg/dL
  - Bedtime glucose steady
Case 3

JAMES
35 YEAR OLD MALE
TYPE 1
HBA1C = 7.3%

BMI: 22
HT: 5'11"
WT: 163lbs

DIABETES DIAGNOSIS:
T1 for 22 years, A1c 7.3%

OTHER MEDICAL CONDITIONS:
None

DM MEDS:
Basal insulin at bedtime.
Rapid-acting insulin before each meal (uses a carb-to-insulin ratio) & for high glucose corrections (correction factor).

GLUCOSE MONITORING:
Usually checks BG before meals, before/after exercise, at bedtime, and if he suspects hypoglycemia.

REASON FOR SENSOR MONITORING:
Complains of frequent, unexpected afternoon hypoglycemia.

* Patient portrayal. This case study is not an actual patient portrayal and is intended for educating healthcare professionals only. © 2015 Abbott. ADC-01953 Ver 2.0 10/15

Lynne K. Lyons, MPH, RD, CDE
Scientific Affairs Manager, Scientific Affairs Department
Case 3

Estimated A1c 7.3%

Glucose mg/dL 162

Daily Average

<table>
<thead>
<tr>
<th>12am</th>
<th>2am</th>
<th>4am</th>
<th>6am</th>
<th>8am</th>
<th>10am</th>
<th>12pm</th>
<th>2pm</th>
<th>4pm</th>
<th>6pm</th>
<th>8pm</th>
<th>10pm</th>
<th>12am</th>
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<tbody>
<tr>
<td>186</td>
<td>175</td>
<td>165</td>
<td>151</td>
<td>168</td>
<td>150</td>
<td>135</td>
<td>129</td>
<td>152</td>
<td>156</td>
<td>170</td>
<td>203</td>
<td></td>
</tr>
</tbody>
</table>

Target Range 85 to 130

25th to 75th Percentile

10th to 90th Percentile

Median
Case 4

**LUCY**

66 year old female
Type 2
HbA1c = 7.1%

**BMI:** 32

**Diabetes Diagnosis:**
T2 for 8 years,
A1c 7.1%

**Other Medical Conditions:**
Hyperlipidemia, hypertension, irritable bowel syndrome, Hx of MI with CABG, stage 3 CKD with GFR: 45 mL/min.

**DM Meds:**
Biphasic insulin aspart
70/30 (BIAsp 70/30).
12 units at 0630;
15 units at 1800.

**Glucose Monitoring:**
Checks BG BID 0600 and 1730. Usually < 160 mg/dL.

**Reason for Sensor Monitoring:**
Complains of encountering low glucose when she attempts to keep levels in range of 85-130 mg/dL, afraid of deteriorating kidney function and wants assurance that her readings are "keeping kidneys safe."
Estimated A1c 7.1%

<table>
<thead>
<tr>
<th>Time</th>
<th>Glucose (mg/dL)</th>
<th>Target Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>12am</td>
<td>153</td>
<td>130-150</td>
</tr>
<tr>
<td>2am</td>
<td>141</td>
<td>130-150</td>
</tr>
<tr>
<td>4am</td>
<td>142</td>
<td>130-150</td>
</tr>
<tr>
<td>6am</td>
<td>153</td>
<td>130-150</td>
</tr>
<tr>
<td>8am</td>
<td>162</td>
<td>130-150</td>
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<tr>
<td>10am</td>
<td>186</td>
<td>130-150</td>
</tr>
<tr>
<td>12pm</td>
<td>154</td>
<td>130-150</td>
</tr>
<tr>
<td>2pm</td>
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<td>148</td>
<td>130-150</td>
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<td>6pm</td>
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<td>10pm</td>
<td>168</td>
<td>130-150</td>
</tr>
<tr>
<td>12am</td>
<td></td>
<td>85-130</td>
</tr>
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Case 4

Estimated A1c 7.1%
Conclusion

- CGM is a relatively new concept, but has become more available
- Accuracy is acceptable and reliable
- Data with A1C reduction
- Data with hypoglycemia reduction
- Safe and minimally invasive
- Many other use for CGM
- Encourage and facilitate lifestyle modification
- CGM should be considered as a potent non-pharmacological treatment for patients with T1D and T2D
Questions