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Using Continuous Glucose Monitoring (CGM) System Data to Assess and Improve Glucose Control
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UC health system diabetes coordinator
Assistant Clinical Professor Skaggs School of Pharmacy and Health Sciences
San Diego, California

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

• Conflict of Interest (COI) and Financial Relationship Disclosures:
  – Presenter: Panteha Kelly, RPh, CDE – No COI/Financial Relationship to disclose

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• Off-Label Use:
  – Participants will be notified by speakers if any product used for a purpose other than for which it was approved by the Food and Drug Administration.
Objective
• Compare and contrast blood glucose meter and continuous glucose monitoring (CGM) data
• Describe the differences between CGM systems
• Interpret CGM data to correctly adjust insulin dose
• Discuss the correlation between CGM results and A1C values
• Identify candidates for CGM use
• Identify Medicare eligibility requirements for approval
• Explain cost of available CGM devices and private insurance eligibility

Mary
Mary is 77 year-old female with history of type 2 diabetes for the past 30 years. She is referred to your clinic for diabetes education and therapy management. She is a retired nurse and lives with her husband.

Insurance: Medicare A&B and secondary United Health Care

Labs:
- HgbA1C: 12%
- GFR: 46 ml/min
- Microalb/Creat ratio: 57 mcg/mg
- TC: 173
- TG: 208
- LFT: WNL
- BMI: 39.9
Mary

- Does not like to check her blood glucose because “it hurts”
- She would like to obtain Freestyle Libre advertised on TV
- Her goal is to lose 20 lbs and to get her blood glucose under control
- Reports she has “sweet tooth” and usually has some sweets at home
- She would like to get a dietary consult on how to lose weight
- Exercises with her trainer everyday for 1 hour at the gym from 9-11am

Medications

- glargine-lixisenatide
  34 units daily
- Aspart insulin 5 units with lunch and dinner also 1 unit with snacks that contain high carbohydrate such as cookies, cakes, ice-cream etc.

Is CGM a suitable device for this person with diabetes?

A GOOD QUESTION THAT IS
Fingerstick Measurement
Measured by blood glucose meter

Interstitial Fluid Glucose Measurement
Measured by Continuous Glucose Monitor

Available CGM Systems

**Professional CGM Systems**
- Abbott Freestyle Libre Pro system
- Medtronic iPro2 Enlite sensor and recorder

**Personal CGM Systems**
- Abbott FreeStyle Libre sensor and reader
- Dexcom Platinum G4/Dexcom Mobile G5 sensor and G4 or G6 transmitter
- Dexcom G6 sensor and transmitter
- Medtronic Enlite sensor and MiniLink or Guardian Link transmitter
- Medtronic Guardian Sensor 3 and Guardian Link 3 transmitter
- Eversense implantable sensor and transmitter

Eversense
FreeStyle Libre
Dexcom G6
Dexcom G5
Guardian Link
CGM Comparison

Real time vs Intermittent Scan /Flash CGM

<table>
<thead>
<tr>
<th></th>
<th>CGM Duration of sensor wear (days)</th>
<th>Start-up time (minute)</th>
<th>Calibration requirement</th>
<th>Trend arrows</th>
<th>Alarm and Alerts</th>
<th>iCloud Sharing</th>
<th>Smart phone use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Realtime CGM</td>
<td>7-10</td>
<td>60-120</td>
<td>Some devices</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Flash CGM</td>
<td>14</td>
<td>60</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Yes (only iPhone 7 or more)</td>
</tr>
</tbody>
</table>

Patient Selection for CGM

Preferred rtCGM
- T1D
- Nocturnal hypoglycemia or unawareness
- On CSII
- Persons with diabetes who have severe fear of hypoglycemia
- Visually impaired or have dexterity problem
- Pregnant women with diabetes

rtCGM or isCGM
- T2D on insulin
- Any individual who has elevated A1C and are not adherent to medications or insulin and do not monitor blood glucose

Pros and Cons of Glucose meters vs. Intermittent Scan Continuous Glucose Monitor

Glucose meter
- Requires to perform fingerstick
- The fingerstick can negatively influence individual
- Must not be feasible at work or school
- It is susceptible to poor testing technique
- Inadequate blood sample or contamination
- It only measures glucose at a single point in time and does not give any indication of the direction and rate of change
- Cannot detect impending hypoglycemia
- Nocturnal and asymptomatic hypoglycemia can go undetected
- Accurate measure of blood glucose at a point in time

Intermittent Scan Continuous Glucose Monitor (isCGM)
- Does not require fingerstick
- Requires scanning the reader over the sensor
- Does not alert of hypo or hypoglycemia unless scanned
- Contains blood glucose trend arrow allowing to accurately determine the direction and rate of blood glucose change
- Can show an overview of the pattern of the blood glucose throughout the day
- Can be worn up to 14 days
- Requires 2 hours cooling period after applying new sensor
- Does not need calibration
- iPhone 7 or newer can be used as a reader
- Does not require glucose meter reading
Should Mary start on a CGM?

### CGM Studies on Adults with Type 2 Diabetes

<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>Primary Outcome/Type of CGM</th>
<th>A1C Outcomes</th>
<th>Hypoglycemia Change/Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beck et al.</td>
<td>Adults with T2D on MDI or MDI plus OAD</td>
<td>A1C reduction/beamcom SEVEN</td>
<td>Adjusted mean A1C difference: -0.3%, P=0.022</td>
<td>No change in hypoglycemia</td>
</tr>
<tr>
<td>Ehrhardt et al.</td>
<td>Adults with T2D not on prandial insulin (half OAD alone)</td>
<td>A1C reduction/beamcom SEVEN</td>
<td>Difference in A1C: -0.6%, P=0.002</td>
<td>Hypoglycemia data NA</td>
</tr>
</tbody>
</table>


### CGM Studies on Adults with Type 1 & 2 Diabetes

<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>Primary Outcome/Type of CGM</th>
<th>A1C Outcomes</th>
<th>Hypoglycemia change/other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haak et al.</td>
<td>Adults with T2D on prandial-only insulin on MDI or CGM</td>
<td>A1C reduction/Beamcom Libre</td>
<td>No difference in A1C overall; difference in A1C if &lt;65 years of age, P=0.03</td>
<td>Time in hypoglycemia (&lt;70mg/dL) was reduced by 43%, P=0.0006</td>
</tr>
<tr>
<td>Garg et al.</td>
<td>Adults with T1D or T2D on insulin</td>
<td>Time spent in high, low, and target glucose zones/beamcom STS sensor</td>
<td>23% less time in hypoglycemia (&lt;55mg/dL)</td>
<td>CGM group spent 21% less time in hypoglycemia (&lt;55mg/dL); P=0.0001</td>
</tr>
</tbody>
</table>

CGM Data Interpretation

• Wearing a CGM alone will not improve blood glucose
• Engaging users in interpreting their CGM data empowers them to respond appropriately to extreme glycemic excursions and effectively manage their diabetes
• Clinicians should understand how to interpret the retrospective CGM data to effectively guide persons with diabetes in their diabetes management journey
• Diabetes Educators should assist individuals with appropriate CGM selection, initiation and education on advanced pattern management skills and also provide an ongoing support to keep individuals engage on their diabetes management

FreeStyle Libre Software

Dexcom G5/6 Software

LibreView
CGM Glucose Pattern Summary

- Average Glucose: 169 mg/dL
- Time In Range: 62%
- Above 180 mg/dL: 37%
- Below 70 mg/dL: 1%
- Coefficient of Variation (CV): 26.7%
- Standard Deviation (SD): 45.2 mg/dL

*Reference ranges calculated from population without diabetes

Ambulatory Glucose Profile (AGP)

Curves depict normogluucose frequency distributions by time regardless of data
Take Home Message for AGP Interpretation

- A minimum of 10-14 days is needed for adequate decision making
- Good goal for hypoglycemia:
  - ≤3% of the day at <70mg/dL (<3.9mmol/L)
  - ≤1% of the day at <54mg/dL (<3.0mmol/L)
- Coefficient variation (CV) is a metric that determines the level of glycemic variability. This indicator is important as it correlates with future diabetes complications, such as nephropathy and CVD
  - The stable glycemic variability is <36%
- Glucose management indicator (GMI): new terminology replacing A1C
  - It is from CGM derived mean glucose to an estimated current A1C

Mary's CGM Glucose overview

<p>| | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Average Glucose</strong></td>
<td><strong>Time in Range</strong></td>
<td><strong>Coefficient of Variation (CV)</strong></td>
</tr>
<tr>
<td>198 mg/dL</td>
<td>≤60 mg/dL</td>
<td>27.7 %</td>
</tr>
<tr>
<td>68-181 mg/dL</td>
<td></td>
<td>54.9 %</td>
</tr>
<tr>
<td>80-120 mg/dL</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Mary’s 2 week’s FCGM results

How Does CGM Data Correlates with A1C Values?

Glucose Management Indicator (GMI)
- It is a new term for estimating A1C (eA1C) from continuous glucose monitoring
- GMI (%) is calculated from average CGM glucose, which measures glucose in interstitial fluid every 1-5 minutes
- There are clinical scenarios that GMI and laboratory values don’t agree with one another.
- There are certain medical conditions that can affect the life span of red blood cells that can explain the differences between laboratory A1C value and GMI such as hemoglobinopathies and hemolytic anemia
Factors Affecting A1C values

- Uremia
- Anemia
- Hemoglobinopathies
- Persistent fetal hemoglobin
- Pregnancy
- Hemodialysis
- Alcohol
- Aspirin

Glucose management indicator (GMI)

<table>
<thead>
<tr>
<th>CGM-derived mean glucose (mg/dL)</th>
<th>GMI (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>70</td>
<td>5.7</td>
</tr>
<tr>
<td>85</td>
<td>6.3</td>
</tr>
<tr>
<td>95</td>
<td>6.9</td>
</tr>
<tr>
<td>105</td>
<td>7.5</td>
</tr>
<tr>
<td>115</td>
<td>8.1</td>
</tr>
<tr>
<td>125</td>
<td>8.7</td>
</tr>
<tr>
<td>135</td>
<td>9.3</td>
</tr>
<tr>
<td>145</td>
<td>9.9</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>CGM-measured mean glucose (mmol/L)</th>
<th>GMI (mmol/mol)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>36.2</td>
</tr>
<tr>
<td>6</td>
<td>40.9</td>
</tr>
<tr>
<td>7</td>
<td>45.7</td>
</tr>
<tr>
<td>8</td>
<td>50.4</td>
</tr>
<tr>
<td>9</td>
<td>55.1</td>
</tr>
<tr>
<td>10</td>
<td>59.8</td>
</tr>
<tr>
<td>12</td>
<td>69.2</td>
</tr>
<tr>
<td>14</td>
<td>78.6</td>
</tr>
<tr>
<td>16</td>
<td>88.0</td>
</tr>
</tbody>
</table>

Correlation between Time in Range (TIR) and A1C Achieved

<table>
<thead>
<tr>
<th>Time in Range (TIR) (%)</th>
<th>HbA1C (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>12.1</td>
</tr>
<tr>
<td>10</td>
<td>11.4</td>
</tr>
<tr>
<td>20</td>
<td>10.6</td>
</tr>
<tr>
<td>30</td>
<td>9.8</td>
</tr>
<tr>
<td>40</td>
<td>9.0</td>
</tr>
<tr>
<td>50</td>
<td>8.3</td>
</tr>
<tr>
<td>60</td>
<td>7.5</td>
</tr>
<tr>
<td>70</td>
<td>6.7</td>
</tr>
<tr>
<td>80</td>
<td>5.9</td>
</tr>
<tr>
<td>90</td>
<td>5.1</td>
</tr>
<tr>
<td>100</td>
<td>4.3</td>
</tr>
</tbody>
</table>
Differences between A1C and GMI

<table>
<thead>
<tr>
<th>Laboratory A1C</th>
<th>GMI Results</th>
<th>Reasons</th>
<th>Plan</th>
</tr>
</thead>
<tbody>
<tr>
<td>8.0%</td>
<td>7.8%</td>
<td>A1C similar to GMI</td>
<td>Average CGM blood glucose is what would be predicted from measured A1C. Plan the management as needed to patient's fasting goal.</td>
</tr>
<tr>
<td>8.0%</td>
<td>7.2%</td>
<td>A1C &gt; GMI</td>
<td>During the short periods of much lower values of glucose reading (starting a much lower CHO reduced diet, an intensive exercise, starting a new diabetes agents that is very effective in reducing BG) Plan a higher A1C goal for patient as there maybe excessive hypoglycemic episodes during the day or week Goal &lt;3% in 70 mg/dL Goal &lt;1% in 54 mg/dL</td>
</tr>
<tr>
<td>7.2%</td>
<td>8.0%</td>
<td>A1C &lt; GMI</td>
<td>During short periods of acute hyperglycemia (DKA, steroid administration, stress) No to set high A1C goal for patient.</td>
</tr>
</tbody>
</table>

Mary's treatment goal

- Current A1C 12%
- Average BG is 198
- GMI is 8.1%
- A1C > GMI
- TIR: 40% hence current A1C is 9.0%
- Individual experiences hypoglycemia hence higher A1C goal would be warranted.
- Selected A1C range 6.3-8.3%. Given individual’s comorbid conditions and age, appropriate A1C is 8.3%

What Do Trend Arrows Mean and How can we use them?
Trend Arrow Usage

- Allows the user to determine the direction of blood glucose.
- Trend arrows correspond to different rates of glucose change depending on the brand of CGM system.
- It can be used to adjust insulin dosage.
- Flash CGMs BG trends have a large margin of error for glucose below 70 mg/dl and above 250 mg/dl. Fingerstick BG should be obtained for accurate BG reading.
- For individuals on bolus insulin, the rise of trend arrow allows the patient to be proactive in correcting BG rise.
- The use of trend arrows before exercise allows the user to be proactive to prevent hypoglycemia by consuming a small snack before the activity.


**Trend Arrow Methods for Insulin Dose Adjustment**

<table>
<thead>
<tr>
<th>Trend Arrow</th>
<th>Petits and Edelman</th>
<th>Endocrine Society (Dexcom G5 only)</th>
</tr>
</thead>
<tbody>
<tr>
<td>🡒ië</td>
<td>+200 mg/dl</td>
<td>+1.5-4.5 based on Correction factor (CF)</td>
</tr>
<tr>
<td>🡒</td>
<td>+75 mg/dl</td>
<td>+0.5-3.5 based on CF</td>
</tr>
<tr>
<td>🡒</td>
<td>+50 mg/dl</td>
<td>+0.5-2.5 based on CF</td>
</tr>
<tr>
<td>No Change</td>
<td>No change</td>
<td></td>
</tr>
<tr>
<td>⬇</td>
<td>-50 mg/dl</td>
<td>-0.5-2.5 based on CF</td>
</tr>
<tr>
<td>⬇</td>
<td>-75 mg/dl</td>
<td>-1-3.5 based on CF</td>
</tr>
<tr>
<td>⬇</td>
<td>-100 mg/dl</td>
<td>-1.5-4.5 based on CF</td>
</tr>
</tbody>
</table>
FreeStyle Libre Trend Arrow Insulin Dose Adjustment

<table>
<thead>
<tr>
<th>Trend Arrow</th>
<th>Freestyle Trend Direction</th>
<th>Glucose Change Factor (mg/dL)</th>
<th>Insulin Dose Adjustment (Units)</th>
</tr>
</thead>
<tbody>
<tr>
<td>↑</td>
<td>Glucose is rising quickly (&gt;2 mg/dL per min)</td>
<td>&lt;25</td>
<td>+2</td>
</tr>
<tr>
<td>↑</td>
<td>Glucose is rising (0.5-1 mg/dL per min)</td>
<td>25-50</td>
<td>+1</td>
</tr>
<tr>
<td>↑</td>
<td>Glucose is rising slowly (&lt;0.5 mg/dL per min)</td>
<td>&gt;50</td>
<td>No change</td>
</tr>
<tr>
<td>↓</td>
<td>Glucose is falling (&gt;2 mg/dL per min)</td>
<td>&lt;25</td>
<td>–2</td>
</tr>
<tr>
<td>↓</td>
<td>Glucose is falling (1-2 mg/dL per min)</td>
<td>25-50</td>
<td>–1</td>
</tr>
<tr>
<td>↓</td>
<td>Glucose is falling slowly (&lt;1 mg/dL per min)</td>
<td>&gt;50</td>
<td>No change</td>
</tr>
</tbody>
</table>

Key Variables to Consider When Using ROC Arrows

- Variability of insulin onset, peak action, and duration
- Impact of meal composition and portion size
- Prior and anticipated exercise taking into account the duration and intensity
- Medications that raise the glucose values
- Stress level
- Illness

Mary is confused as her blood glucose reading is very different from her CGM glucose data

Is CGM Data Accurate?
How Reliable are the Data from CGM?

CGM Accuracy

MARD: Mean Absolute Relative Differences
- It is a key accuracy measurement for CGM systems
- It compares CGM readings to reference values obtained from blood glucose measurements form a laboratory analyzer, typically the Yellow Springs Instruments (YSI)
- If the YSI reading= 150 mg/dL and CGM reading= 120 mg/dL, the system has a 20% MARD (30/150=20%)
- Differences in study protocols and procedures have made it difficult to compare the accuracy of different systems
- MARD Values have improved from >20% to <10% over the past decade

MARD Comparison among CGMs

<table>
<thead>
<tr>
<th>CGM Systems</th>
<th>MARD, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abbott FreeStyle Libre Pro sensor</td>
<td>12.3</td>
</tr>
<tr>
<td>Medtronic iPro2 Elite sensor</td>
<td>13.6</td>
</tr>
<tr>
<td>Abbott Freestyle Libre sensor</td>
<td>9.7</td>
</tr>
<tr>
<td>Dexcom Platinum G4/G5 sensor with most current Dexcom software</td>
<td>9.0</td>
</tr>
<tr>
<td>Dexcom G6 sensor</td>
<td>9.0</td>
</tr>
<tr>
<td>with no calibrations</td>
<td></td>
</tr>
<tr>
<td>Medtronic Enlite sensor</td>
<td>13.6</td>
</tr>
<tr>
<td>Medtronic Guardian Sensor 3 sensor</td>
<td>9.6 with 3-4 calibrations per day; 10.6 with 2 calibrations per day</td>
</tr>
<tr>
<td>Eversense implantable sensor</td>
<td>8.5</td>
</tr>
</tbody>
</table>
Can I Bill Medicare or Commercial Third Parties for CGM initiation and data analysis?

Billing Requirements:

- All participants with type 1 diabetes:
  - Some require PA but will be covered.
- EMR documentation for CGM Medicare Coverage:
  - Diagnosed at T1 or T2
  - On pump or basal/bolus insulin
  - Checks BG 3-4 times or more
  - Has hypoglycemic unawareness
  - Above information documented in 2 of individual’s encounters
  - Adjust insulin dose based on blood glucose reading
  - The data cannot be added to the medication order
- Most insurance covers under above info has been verified.
- Medicaid payment for CGM coverage in each state is different.
Current CPT code for Reimbursement

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
<th>Who can perform and bill for service</th>
<th>Medicare Physician Fee Schedule</th>
<th>Medicare Outpatient Diabetes Center</th>
<th>Private Payer (2018)</th>
</tr>
</thead>
<tbody>
<tr>
<td>95249</td>
<td>Initiation of person’s own CGM</td>
<td>RN, Pharm/D/RPh, RD, CDE or MA</td>
<td>$96.56</td>
<td>$95.96</td>
<td>$132</td>
</tr>
<tr>
<td>95250</td>
<td>Initiation of CGM; clinician owned equipment</td>
<td>RN, Pharm/D/RPh, RD, CDE or MA</td>
<td>$198.58</td>
<td>$113.69</td>
<td>$300</td>
</tr>
<tr>
<td>95251</td>
<td>Interpretation of CGM data</td>
<td>Only MD/DO, NP, PA</td>
<td>$36.72</td>
<td>Paid under the physician fee schedule</td>
<td>$89</td>
</tr>
</tbody>
</table>

What Does the Person with Diabetes Needs to Know?

- How to apply and start their CGMs
- Importance of consistent wear of the device
- For FreeStyle Libre, frequent scanning of the sensor
- Accuracy of the CGMs in compare to actual Blood Glucose measurements
- Educating individuals on how to interpret their results once downloaded
- How the trend arrow works and how to use them to adjust insulin dosage

Role of Diabetes Educator

- Identify the most suitable CGMs for individuals with diabetes
- Educate individuals on the features of the device
- Educate individuals on how to apply and use the device
- Discuss the accuracy of the data obtained by the device and the importance of fingerstick BG when needed