Continuous Glucose Monitoring (CGM)
Background Info

• A1c
  • Average glucose levels over previous 2-3 months
  • Currently remains gold standard for determining control
  • Indicator of risk for development of complications
  • Limitations
    • Does not provide data as to how to adjust therapy when the A1c is elevated
    • Does not detect hypoglycemia or hyperglycemia on a daily basis
    • Unreliable measurements in those with anemia or hemoglobinopathies
    • Does not detect rapid changes in daily glucose control
CGM: Continuous Glucose Monitor
- CGMs do not take blood sugar readings but reading interstitial
  - Algorithm used to adjust for blood glucose
  - Record reading every 5 minutes

CGM Advantages
- Intra- and interday glycemic excursions evaluations
- Hypo- and hyperglycemic prediction
- A1c reductions
- Increase time in goal range
- Decrease time below goal range

2 types of CGMs
- Blinded
  - Patient does not see the blood sugar number
CGM Types

- **Unblinded** – patient does see the blood sugar reading
  - Available for both professional setting and personal setting
  - Real-time CGM
    - Unblinded glucose data and trends
    - Unblinded direction and rate of change
    - Alerts/alarms warning user or high/low
  - Studies suggest:
    - Improved quality of life for both children and adults
    - Improved A1c
    - Lessened time in hypo- and hyperglycemia ranges
    - Reduced moderate – severe hypoglycemia occurrence
    - Sensor-augmented pump therapy is cost-effective
CGM Types

- Intermittently viewed CGM
  - Two components: sensor and reader
  - Provides current glucose plus retrospective data
    - Transmits 8 hours of data with each scan
  - “Flash” monitoring
  - Currently: No alarms
  - User is still driving the monitoring
- Studies suggest
  - Less hypoglycemia
  - Improved time in range
  - Improved glycemic variability
  - User satisfaction
Pieces and Parts

Three parts:
1. Sensor
2. Transmitter
3. Display Device
Differences between CGMs

• Warm up period
• Accuracy
• Number of Calibrations if any required
• Stand alone or interface with pump
• How far in advance it predicts highs/lows
• Alerts
• Sharing capability
• Medicare coverage
• Insertion of sensor (Dexcom’s new applicator has been approved)
CGM Types - Manufactures

- Abbott
  - Freestyle LibrePro – Professional
    - Blinded
    - No calibrations
    - 14 day wear
  - FreeStyle Libre-Personal
    - Intermittently viewed via Touch screen
    - No calibrations
    - 10 day wear
    - FDA approved to make treatment decisions
    - Wear on back of upper arm
### CGM Types - Manufactures

**Dexcom**

<table>
<thead>
<tr>
<th>G4: Professional and G5: Personal</th>
<th>G6: Personal</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Twice daily Calibrations</td>
<td>• No Calibrations</td>
</tr>
<tr>
<td>• G5 approved treatment decisions</td>
<td>• Approved for treatment decisions</td>
</tr>
<tr>
<td>• Sensor wear for 7 days</td>
<td>• Sensor wear for 10 days</td>
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<tr>
<td>• Placed on abdomen</td>
<td>• Placed on abdomen</td>
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<tr>
<td>• Approved for age 2 and older</td>
<td>• Approved for age 2 and older</td>
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<tr>
<td>• Hypoglycemia alerts (&lt;55mg/dl)</td>
<td>• Alert for prediction of low</td>
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<tr>
<td>• Customizable Alerts for rapid changes</td>
<td>• Customizable Alerts for rapid changes</td>
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</table>
Eversense Continuous Glucose Monitor—

- The sensor is professionally placed in the healthcare providers office via small incision under the skin of the upper arm
- Sensor stays in skin for 90 days
- Removed every 3 months at provider office and new sensor placed on alternate arm
- Transmitter is placed with adherence over the sensor
  - Transmitter will vibrate on skin to alert of low
  - Transmitter can be removed without disrupting or restarting the sensor
- Phone app is the receiver
CGM Types - Manufactures

- Medtronic
  - i-Pro2 – Professional
  - Pumps with CGM capability
    - Medtronic 530G + 630G + MiniMed Revel (stand alone pump + CGM)
    - Medtronic 670G Hybrid closed loop – personal pump with CGM
      - Automatically adjusts basal insulin delivery based on the CGM readings and recent insulin delivery
    - Tandem T:slim X2 +G5
Medtronic pump with CGM
• ADA International Consensus Statement recommends:
  • CGM should be considered in conjunction with A1c for glycemic status assessment and therapy adjustment in:
    • All patients with type 1 diabetes
    • Patient with type 2 diabetes treated with intensive insulin therapy who are not achieving glucose targets, especially if the patient is experiencing problematic hypoglycemia
  • Given the variable adherence to CGM, assess individual readiness for continuing CGM use prior to prescribing.
  • **When prescribing CGM, robust diabetes education, training, and support are required for optimal CGM**
    • ADA/AACE/AADE consensus report: “CGM is primarily a diagnostic technique and cannot be expected to improve glucose control per se anymore than weighing scales can be expected to reduce weight. Without appropriate training, users of CGM may not be able to make optimal usage of the information provided”
42 Factors That Affect BG

<table>
<thead>
<tr>
<th>Food</th>
<th>Biological</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Carbohydrate quantity</td>
<td>20. Insufficient sleep</td>
</tr>
<tr>
<td>2. Carbohydrate type</td>
<td>21. Stress and illness</td>
</tr>
<tr>
<td>3. Fat</td>
<td>22. Recent hypoglycemia</td>
</tr>
<tr>
<td>4. Protein</td>
<td>23. During-sleep blood sugars</td>
</tr>
<tr>
<td>5. Caffeine</td>
<td>24. Dawn phenomenon</td>
</tr>
<tr>
<td>6. Alcohol</td>
<td>25. Infusion set issues</td>
</tr>
<tr>
<td>7. Meal timing</td>
<td>26. Scar tissue and lipodystrophy</td>
</tr>
<tr>
<td>8. Dehydration</td>
<td>27. Intramuscular insulin delivery</td>
</tr>
<tr>
<td></td>
<td>29. A higher glucose level</td>
</tr>
<tr>
<td></td>
<td>30. Periods (menstruation)</td>
</tr>
<tr>
<td></td>
<td>31. Puberty</td>
</tr>
<tr>
<td></td>
<td>32. Celiac disease</td>
</tr>
<tr>
<td></td>
<td>33. Smoking</td>
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</tbody>
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<table>
<thead>
<tr>
<th>Medication</th>
<th>Activity</th>
<th>Environmental</th>
</tr>
</thead>
<tbody>
<tr>
<td>10. Medication dose</td>
<td>15. Light exercise</td>
<td>34. Expired insulin</td>
</tr>
<tr>
<td>12. Medication interactions</td>
<td>17. Level of fitness/training</td>
<td>36. Outside temperature</td>
</tr>
<tr>
<td>13. Steroid administration</td>
<td>18. Time of day</td>
<td>37. Sunburn</td>
</tr>
<tr>
<td>14. Niacin (Vitamin B3)</td>
<td>19. Food and insulin timing</td>
<td>38. Altitude</td>
</tr>
</tbody>
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<table>
<thead>
<tr>
<th>Behavioral &amp; Decision Making</th>
</tr>
</thead>
<tbody>
<tr>
<td>39. Frequency of glucose checks</td>
</tr>
<tr>
<td>40. Default options and choices</td>
</tr>
<tr>
<td>41. Decision-making biases</td>
</tr>
<tr>
<td>42. Family relationships and social pressures</td>
</tr>
</tbody>
</table>
Key Metrics from CGM reports

- Glycemic control and variability will be evaluated from CGM data as well as the following key metrics (data sufficiency defined as 10 of 14 days of data):
  - Ambulatory Glucose Profile (AGP)-provides standardized visualization of BS
    - Mean glucose
    - Estimated A1c
    - Time in Range (defined as 70-180)
    - Time in hypoglycemia range
    - Time in Hyperglycemia range
    - Coefficient of variation (goal <36%)
    - Collection period/data sufficiency
Ambulatory Glucose Profile

- Promotes a standardized presentation of the downloaded data
  - Aides in the identification of patterns, glucose variability and frequency of lows
  - All current CGM’s available are using this profile in their reporting to support consistent visualization and interpretation

- Can you guess the A1c for each patient in the following slide?
- Would you treat each the same?
Ambulatory Glucose Profile

<table>
<thead>
<tr>
<th>Glucose Statistics</th>
<th>Average Glucose mg/dL</th>
<th>Glycemic Estimate</th>
<th>Very Low Below 54</th>
<th>Low Alert Below 70</th>
<th>In Target Range 70-180</th>
<th>High Alert Above 180</th>
<th>Very High Above 250</th>
<th>Active</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Avg Glucose</td>
<td>156</td>
<td>7.0%</td>
<td>4.4%</td>
<td>10.1%</td>
<td>54.5%</td>
<td>35.4%</td>
<td>11.3%</td>
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<tr>
<td></td>
<td>Estimate</td>
<td>88-115</td>
<td>&lt;6 mg/dL</td>
<td>&lt;6 mg/dL</td>
<td>&lt;6 mg/dL</td>
<td>&lt;6 mg/dL</td>
<td>&lt;6 mg/dL</td>
<td>&lt;6 mg/dL</td>
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</table>

<table>
<thead>
<tr>
<th>Glucose Exposure Close-Up</th>
<th>AUC Hourly (mg/dL/mM)</th>
<th>Glucose Exposure Close-Up</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>000</td>
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<table>
<thead>
<tr>
<th>Variability Close-Up</th>
<th>Variability</th>
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<tbody>
<tr>
<td></td>
<td>0.0</td>
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</table>

<table>
<thead>
<tr>
<th>Coefficient of Variation</th>
<th>46.3%</th>
<th>72 mg/dL</th>
<th>70.6%</th>
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<table>
<thead>
<tr>
<th>% Time CGM Active</th>
<th>70.6%</th>
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<thead>
<tr>
<th>Hypoglycemia</th>
<th>Hypoglycemia</th>
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<tbody>
<tr>
<td>0.0</td>
<td>0.0</td>
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<table>
<thead>
<tr>
<th>Hypertension</th>
<th>Hypertension</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.0</td>
<td>0.0</td>
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<tr>
<th>Reference Ranges</th>
<th>Calculated from population without diabetes. Level 1 = Healthy. Level 2 = Intermediate.</th>
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<tr>
<td>Carburetor rates</td>
<td>glucose frequency distributions by time spent of data.</td>
</tr>
</tbody>
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*Reference ranges calculated from population without diabetes. Level 1 = Healthy. Level 2 = Intermediate.*
Taken from: Diabetes Care 2017 Aug; 40(8): 994-999. https://doi.org/10.2337/dc17-0636
Ambulatory Glucose Profile

ALL FOUR PATIENTS HAD AN A1c OF: 8%!!!
Key Metrics:

• Collection Period
  • To maximize use:
    • Benefits are directly related to amount of use
    • Estimated A1c can be calculated with
      • 70% of data for duration of wear
        OR
      • 10 days out of 14 days of data
    • Meta-analysis results:
      • Every 1-day increase of sensor usage per week:
        • Increase CGM efficacy
        • Increased impact of A1c outcomes
      • Cost effective benefits are also correlated with amount of use
Key Metrics

- Time in Range (TIR)
  - ADA has defined target range as:
    - 70-180mg/dL
  - Goal % time in range:
    - Not yet defined
    - Must individualize like A1c goals and factor in:
      - Age
      - Comorbidities
      - Patient adherence
Key Metrics:
A few studies have reported TIR related to A1c outcomes

**Medtronic MiniMed 670G**
- Participants on hybrid closed loop (vs pump users on open loop)
- TIR (71-180 mg/dl): 72% (vs 67%)
- Baseline A1c: 7.4%
- Ending A1c: 6.9%

**IMPACT Study**
- Abbott FreeStyle Libre – participants on both MDI and pumps (vs fingersticks)
- TIR (70-180 mg/dl): 66% (vs. 61%)
  - A decrease of 74 min/day in HYPOglycemia (38% less)
- Baseline A1c: 6.8%
- Ending A1c: ~7%

**DIAMOND Study**
- Dexcom users on MDI (vs fingerstick)
- TIR (70-180 mg/dl): 51% (vs. 45%)
- Baseline A1c: 8.6%
- Ending A1c: 7.7%
Key Metrics

- Glucose variability
  - Both hyper- and hypoglycemic episodes may trigger responses that are:
    - Pro-inflammatory
    - Pro-oxidant
    - Pro-coagulant
  - Research suggests variation in glucose control may be related to adverse outcomes for those with type 2 diabetes but do to lack of standardization with defining variability, the exact impact is still of debate

- Quantifying Glucose Variability
  - Standard deviation (SD)
    - Biased towards hyperglycemia
    - Hyperglycemia deviations are numerically “heavier” than the low ones
      - Thus less sensitive to hypoglycemia
Key Metrics

- Coefficient of variation (CV)
  - CV is preferred reporting metric over SD as it is a metric:
    - Relative to the mean
    - More descriptive for hypoglycemic excursions than the SD alone
  - In conclusion, CV allows assessment of variability that is less influenced by the mean glucose or HbA1c than SD
  - Reported as %CV
    - 36% defined as a “suitable threshold” to determine if glucose values are “stable” vs “unstable”
    - Higher than this suggests the frequency of lows is significantly increased
Patient case: VJ

- 81 year old male with type 2 Diabetes
- PMH: CAD w/ h/o MI, HLD, HTN, sleep apnea, chronic renal insufficiency, anemia, hearing loss, hyperparathyroidism, shingles, PVD and BKA
- Allergies: Rocephin, Advicor, Cipro and PCN
- Tobacco use: (-)
- VS and Labs: BP100/60, Pulse: 60, BS 198, SrCr 1.2, Na 139, K 4.7, LDL 59, HDL 35, TG 79, A1c 7.7%
- Anthropometrics: Weight 211 lbs, BMI 30
- DM Medications:
  - Lantus 18 units SQ QHS
  - Humalog 9-8-9 units with meals
  - Humalog ISF 1 unit for every 50/150
- Patient seen in the medication clinic for review of diabetes and BS log was reviewed with the below findings
- Blood glucose results and trends:
  - Before breakfast - 97, 85, 119, 123, 101, 114, 149, 135, 95, 112, 85, 121, 151, 91, 78, 161, 89 (average 112)
  - Before lunch - 135, 99, 93, 80, 94, 142, 70, 121, 71, 121, 133, 64, 81 (average 100)
  - Before dinner - 122, 62, 99, 131, 91, 81, 142, 205 (big pizza), 314 (18 cookies), 41 (107 after correction), 74, 128, 149, 114, 97, 69, 127, 149, 63 (average 118)
  - Bedtime range - 63, 97, 62, 110, 74, 84, 154, 105, 239, 147, 206, 278, 218, 282, 141 (average 151)
- At end of visit, Pharmacist:
  - Coordinated same day placement of CGM with Diabetes center with medication change
Intervention on D4:
1. Humalog d/c
2. Initiate Victoza SQ daily
Patient case VJ: Follow up CGM
Patient Case #2: Initial CGM Study

Glucose Statistics

- Avg Glucose mg/dL: 184
- Glucose Exposure: 184
- Low: 3.5%
- High: 15.8%
- In Target Range: 47.7%
- Very Low: 1.4%
- Very High: 39.5%
- Coefficient of Variation: 73 mg/dL
- SD mg/dL
- % Time CGM Active: 98.4%

Curves/plots represent glucose frequency distributions by time regardless of date.
Use in Practice

• Recent survey by Diabetes in Control Data: (PiperJaffray diabetes survey (n=339) from Feb 13-26, 2018 consisting of patients, physicians, nurses and CDEs)
  • Surveyed patients, families, doctors, nurses and diabetes educators to gather options on futures role of continuous monitors
  • Survey results
    • Both health care providers AND patients:
      • Strongly expect CGM adoption to group dramatically over the next 5 years
      • Expect CGMs among patients with type 2 diabetes to become more widespread of the next 5 years
      • Believe the main factor that discourages use is cost
      • Regard the ability to see glucose trends over time as the greatest benefit to CGM use
        • Followed by alerts for highs or lows and making their management of the disease easier
    • Of the patients responding in this survey that were not currently on a CGM:
      • 70% expected to switch to a CGM in the future
<table>
<thead>
<tr>
<th>Clinic</th>
<th>Reimbursement Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes Clinic</td>
<td>95250</td>
<td>Professional CGM placement charge by CDE</td>
</tr>
<tr>
<td></td>
<td>95249</td>
<td>Personal CGM placement charge by CDE</td>
</tr>
<tr>
<td>Comprehensive Medication Management Clinic (Pharmacy)</td>
<td>992111-99214</td>
<td>Facility Fee charge by pharmacist via hospital billing for education and medication management</td>
</tr>
<tr>
<td>Provider</td>
<td>95251</td>
<td>Interpretation fee by physician for review and assessment of CGM</td>
</tr>
</tbody>
</table>
Continuous Glucose Monitoring (CGM)
WHAT TO EXPECT

1. PHYSICIAN: PHYSICIAN OFFICE
   - Patient and physician discuss if glucose monitoring study would be beneficial
   - Physician refers the patient for Continuous Glucose Monitoring

2. DIABETES EDUCATOR: DIABETES CENTER
   - Patient meets with Diabetes Educator to place the continuous monitor
   - Diabetes Educator also provides diabetes education services
   - Patient returns continuous monitor to the Diabetes Center as instructed
   - Diabetes Center communicates information to the Medication Management Clinic

3. PHARMACIST: MEDICATION MANAGEMENT CLINIC
   - Medication Clinic contacts patient for appointment
   - Pharmacist educates on medications and discusses findings of the report with patient
   - Pharmacists and patient set plan to target glucose control and meet patient goals
   - Pharmacist communicates plan with physician for review

4. PATIENT BENEFITS
   - Coordinated effort from physician and experts on diabetes and medication to improve health
   - Data suggests continuous glucose monitoring can allow:
     - Better glucose control
     - Improved awareness of lows, especially during sleep
     - Less frequent lows
   - Patient can learn AND see effects on blood sugars from: Diet, Exercise, Stress, Illness, Medications
Citations:


