CONTINUOUS GLUCOSE MONITORING FOR THE INTERNIST

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Adult Endocrinology
Disclosures:

- No conflict of interest
Objectives

- Is it meaningful to use diabetes technology in 2020?
- Explain how continuous glucose monitoring (CGM) works
- Explain how to interpret main aspects of AGP
- Most common and accessible alternatives in Puerto Rico
- Main differences among them
- Cases for discussion
IS IT MEANINGFUL TO USE DIABETES TECHNOLOGY IN 2020?
Glucose Control and Complications (Diabetes Control and Complication Trial, DCCT)

LOWER AIC → LOWER COMPLICATION RISK
How controlled are our patients?

- The majority of young adults in their 20’s do not fully achieve glycemic control until they are 30.

- Only 14 % of registrants between 18 and 25-years old met the recommended 7 % A1c level compared with 30 % of older adults.

Data from 2010-2012

https://myglu.org/articles/recent-findings-from-the-t1d-exchange-clinic-registry
More recent data (2016-2018 cohort)

- Orange: 2010-2012
- Blue: 2016-2018
- No significant improvement in A1C despite CGM/insulin pump/diabetes technology
A1C comparison regardless of insulin delivery method

https://myglu.org/articles/recent-findings-from-the-t1d-exchange-clinic-registry
Continuous Glucose Monitoring and Intensive Treatment of Type 1 Diabetes

P<0.001
3 Month frequency of severe hypoglycemia according to A1C

*Seizure or Loss of Consciousness: 1 or more events in 3 months from subset who completed insulin and device questionnaire

https://myglu.org/articles/recent-findings-from-the-t1d-exchange-clinic-registry
HBA1C pitfalls and interpretation

Table 6.1—Estimated average glucose (eAG)

<table>
<thead>
<tr>
<th>A1C (%)</th>
<th>mg/dL*</th>
<th>mmol/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>59.7</td>
<td>3.4</td>
</tr>
<tr>
<td>6</td>
<td>85.3</td>
<td>5.3</td>
</tr>
<tr>
<td>7</td>
<td>123.8</td>
<td>7.3</td>
</tr>
<tr>
<td>8</td>
<td>174.3</td>
<td>10.3</td>
</tr>
<tr>
<td>9</td>
<td>240.4</td>
<td>13.9</td>
</tr>
<tr>
<td>10</td>
<td>316.4</td>
<td>19.9</td>
</tr>
<tr>
<td>11</td>
<td>402.4</td>
<td>25.4</td>
</tr>
<tr>
<td>12</td>
<td>498.4</td>
<td>31.3</td>
</tr>
</tbody>
</table>

Data in parentheses are 95% CI. A calculator for converting A1C results into eAG, in either mg/dL or mmol/L, is available at professional.diabetes.org/eAG. *These estimates are based on ADAG data of ~2,700 glucose measurements over 3 months per A1C measurement in 507 adults with type 1, type 2, or no diabetes. The correlation between A1C and average glucose was 0.92 (6.7). Adapted from Nathan et al. (6).

Inappropriately Low HbA1c
- Hemolysis
- Certain hemoglobinopathies
- Recent blood transfusion
- Acute blood loss
- Hypertriglyceridemia
- Drugs
- Chronic liver disease

Inappropriately High HbA1c
- Iron deficiency
- Vitamin B12 deficiency
- Alcoholism
- Uremia
- Hyperbilirubinemia
- Drugs

Variable Effect on HbA1c+
- Fetal hemoglobin
- Methemoglobin
- Certain hemoglobinopathies

ABG of 173 mg/dl
A1C by itself does not tell much...

Laboratory measured A1C lacks: actual Average Blood Glucose, Variability and interference with other conditions.
Candidates for CGM technology

- Patient is on MDI of insulin therapy
- Frequent hypoglycemia, nocturnal hypoglycemias and/or unawareness
- Increased glucose variability (discrepancy between FBG, SMBG, A1C)
- Variations in physical activity
- Willing to use CGM in a daily basis
- Willing to assist to a certified diabetes educator for training
- Children
- Seeking insulin pump therapy or already on it
- To document the need for intensifying therapy
2020 AACE Recommends

- Professional CGM devices (those owned by the clinician’s practice) should be considered in patients:
  - who have not reached their glycemic target after 3 months of the initial antihyperglycemic therapy
  - those who require therapy that is associated with risks of hypoglycemia (SU, insulin)

- Personal CGM devices (those owned by the patient) should be considered for:
  - patients who are on intensive insulin therapy (3 to 4 injections/day or on insulin pump)
  - history of hypoglycemia unawareness
  - recurrent hypoglycemia
HOW CONTINUOUS GLUCOSE MONITORING (CGM) WORKS
Traditional “fingerstick” glucose testing

- A. Sensor
- B. Transmitter
- C. Display device
Interstitial Fluid and “Lag Time”

Capillary glucose must diffuse into the interstitial fluid (ISF).

ISF glucose levels may lag capillary levels by 5–15 minutes.

When glucose levels are stable, ISF glucose levels and capillary blood glucose levels are similar.

When glucose is rising: SG likely lower than actual BG.

When glucose is falling: SG likely higher than actual BG.

Sensor Accuracy – improving over time

MARD: average difference between sensor glucose and YSI

<table>
<thead>
<tr>
<th>Sensor</th>
<th>MARD</th>
</tr>
</thead>
<tbody>
<tr>
<td>MiniMed iPro retrospective CGM</td>
<td>26%</td>
</tr>
<tr>
<td>GlucoWatch</td>
<td>22%</td>
</tr>
<tr>
<td>Original Dexcom</td>
<td>21.2%</td>
</tr>
<tr>
<td>Medtronic Soft Sensor</td>
<td>18.4%</td>
</tr>
<tr>
<td>Dexcom 7 Plus</td>
<td>16%</td>
</tr>
<tr>
<td>Medtronic Enlite</td>
<td>15.3%</td>
</tr>
<tr>
<td>Dexcom G4</td>
<td>13%</td>
</tr>
<tr>
<td>FreeStyle Libre</td>
<td>11.4%</td>
</tr>
<tr>
<td>Medtronic Guardian 3</td>
<td>10%</td>
</tr>
<tr>
<td>Dexcom G5</td>
<td>9%</td>
</tr>
<tr>
<td>Senseonics Eversense</td>
<td>9.4%</td>
</tr>
<tr>
<td>Dexcom G6*</td>
<td>9%</td>
</tr>
</tbody>
</table>
Clinical Targets for Continuous Glucose Monitoring Data Interpretation: Recommendations From the International Consensus on Time in Range

Diabetes Care 2019;42:1593–1603 | https://doi.org/10.2337/dc19-0028
Device-Driven Diabetes Management

International consensus on **TIME IN RANGE** standardized CGM metrics
More Actionable
Guiding medical nutrition therapy and physical activity
Prevent Hypoglycemia

<table>
<thead>
<tr>
<th>Table 6.2—Standardized continuous glucose monitoring (CGM) metrics for clinical care</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Number of days CGM device is worn (recommend 14 days)</td>
</tr>
<tr>
<td>2. Percentage of time CGM device is active (recommend 70% of data from 14 days)</td>
</tr>
<tr>
<td>3. Mean glucose</td>
</tr>
<tr>
<td>4. Glucose management indicator (GMI)</td>
</tr>
<tr>
<td>5. Glycemic variability (%CV) target ≤36%*</td>
</tr>
<tr>
<td>6. Time above range (TAR): % of readings and time &gt;250 mg/dL (&gt;13.9 mmol/L)</td>
</tr>
<tr>
<td>7. Time above range (TAR): % of readings and time 181–250 mg/dL (10.1–13.9 mmol/L)</td>
</tr>
<tr>
<td>8. Time in range (TIR): % of readings and time 70–180 mg/dL (3.9–10.0 mmol/L)</td>
</tr>
<tr>
<td>9. Time below range (TBR): % of readings and time 54–69 mg/dL (3.0–3.8 mmol/L)</td>
</tr>
<tr>
<td>10. Time below range (TBR): % of readings and time &lt;54 mg/dL (&lt;3.0 mmol/L)</td>
</tr>
</tbody>
</table>

*CGM, continuous glucose monitoring; CV, coefficient of variation. *Some studies suggest that lower %CV targets (<33%) provide additional protection against hypoglycemia for those receiving insulin or sulfonylureas. Adapted from Battelino et al. (17).
AGP (Ambulatory Glucose Profile)

**AGP Report**

### GLUCOSE STATISTICS AND TARGETS

<table>
<thead>
<tr>
<th>Date Range</th>
<th>Days Active</th>
<th>% Time CGM is Active</th>
</tr>
</thead>
<tbody>
<tr>
<td>26 Feb 2019-10 Mar 2019</td>
<td>13 days</td>
<td>99.9%</td>
</tr>
</tbody>
</table>

**Glucose Ranges**

- **Target Range:** 70–180 mg/dL
  - Greater than 70% (16h 48min)
- Below 70 mg/dL: Less than 4% (58min)
- Below 54 mg/dL: Less than 1% (14min)
- Above 180 mg/dL: Less than 25% (6h)
- Above 250 mg/dL: Less than 5% (1h 12min)

Each 5% increase in time in range (70–180 mg/dL) is clinically beneficial.

**Average Glucose:** 173 mg/dL  
**Glucose Management Indicator (GMI):** 7.6%  
**Glucose Variability:** 49.5%

**TIME IN RANGES**

- **Very High:** (>250 mg/dL)  
- **High:** (181—250 mg/dL)  
- **Target Range:** (70—180 mg/dL)  
- **Low:** (54—69 mg/dL)  
- **Very Low:** (<54 mg/dL)

- **Very High:** 20% (4h 48min)
- **High:** 23% (5h 31min)
- **Target Range:** 47% (11h 17min)
- **Low:** 4% (58min)
- **Very Low:** 6% (1h 26min)
We may personalize individual glycemic targets.
Variabilidad

Hypoglycemia

Hyperglycemia

AMBULATORY GLUCOSE PROFILE (AGP)

AGP is a summary of glucose values from the report period, with median (50%) and other percentiles shown as if occurring in a single day.

DAILY GLUCOSE PROFILES

Each daily profile represents a midnight-to-midnight period.
AMBULATORY GLUCOSE PROFILE (AGP)

AGP is a summary of glucose values from the report period, with median (50%) and other percentiles shown as if occurring in a single day.

DAILY GLUCOSE PROFILES

Each daily profile represents a midnight-to-midnight period.
Glucose Management Indicator (GMI) aka Real time A1C

- 25 y/o using Dexcom CGM with Hba1c of 8.2%, Hb of 10 g/dl, Hct 31%
- Patient note with glycation gap due to iron deficiency anemia
- Up to 15% of glycated hemoglobin may be misleading in clinical practice
- GMI lower that lab A1C, means glucose is lower that reported by lab and caution is needed in order to avoid hypoglycemia
- Plan: iron supplements to correct anemia, NO INSULIN optimization

<table>
<thead>
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<th>Table 6.1—Estimated average glucose (eAG)</th>
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<tr>
<td><strong>A1C (%)</strong></td>
</tr>
<tr>
<td>5</td>
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<td>10</td>
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<td>11</td>
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<tr>
<td>12</td>
</tr>
</tbody>
</table>

*Her average glucose is not contained in the 95%CI for HBA1C of 8.2%*
## Benefits of Time in Range

Table 5—Estimate of A1C for a given TIR level based on type 1 diabetes and type 2 diabetes studies

<table>
<thead>
<tr>
<th>TIR 70–180 mg/dL (3.9–10.0 mmol/L)</th>
<th>A1C, % (mmol/mol)</th>
<th>95% CI for predicted A1C values, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>20%</td>
<td>9.4 (79)</td>
<td>(8.0, 10.7)</td>
</tr>
<tr>
<td>30%</td>
<td>8.9 (74)</td>
<td>(7.6, 10.2)</td>
</tr>
<tr>
<td>40%</td>
<td>8.4 (68)</td>
<td>(7.1, 9.7)</td>
</tr>
<tr>
<td>50%</td>
<td>7.9 (63)</td>
<td>(6.6, 9.2)</td>
</tr>
<tr>
<td>60%</td>
<td>7.4 (57)</td>
<td>(6.1, 8.8)</td>
</tr>
<tr>
<td>70%</td>
<td>7.0 (53)</td>
<td>(5.6, 8.3)</td>
</tr>
<tr>
<td>80%</td>
<td>6.5 (48)</td>
<td>(5.2, 7.8)</td>
</tr>
<tr>
<td>90%</td>
<td>6.0 (43)</td>
<td>(4.7, 7.3)</td>
</tr>
</tbody>
</table>

Table 5 continued:

<table>
<thead>
<tr>
<th>TIR 70–180 mg/dL (3.9–10.0 mmol/L)</th>
<th>A1C, % (mmol/mol)</th>
</tr>
</thead>
<tbody>
<tr>
<td>20%</td>
<td>10.6 (92)</td>
</tr>
<tr>
<td>30%</td>
<td>9.8 (84)</td>
</tr>
<tr>
<td>40%</td>
<td>9.0 (75)</td>
</tr>
<tr>
<td>50%</td>
<td>8.3 (67)</td>
</tr>
<tr>
<td>60%</td>
<td>7.5 (59)</td>
</tr>
<tr>
<td>70%</td>
<td>6.7 (50)</td>
</tr>
<tr>
<td>80%</td>
<td>5.9 (42)</td>
</tr>
<tr>
<td>90%</td>
<td>5.1 (33)</td>
</tr>
</tbody>
</table>

every 10% increase in TIR = ~0.5% (5.5 mmol/mol) A1C reduction

every 10% increase in TIR = ~0.8% (8.7 mmol/mol) A1C reduction

The difference between findings from the two studies likely stems from differences in number of studies analyzed and subjects included (RCTs with subjects with type 1 diabetes vs. RCTs with subjects with type 1 or type 2 diabetes with CGM and SMBG).

https://care.diabetesjournals.org/content/diacare/42/8/1593.full.pdf
Ambulatory Glucose Profile works if:

• Data can be effectively downloaded for each patient visit
  • Limitations in software, hardware, TIME! or even having the device present

• Data can be effectively interpreted
  • Assess patent routine, wake and sleep times, feedings, medication intake
  • Ask the patient to remember exactly what he was doing for a specific hypoglycemia event in that 14 day log
  • Discuss times of the day where more glucose fluctuations (variability) exist

• Physician and Patient design a course of action (simple solutions are always better!)
  • Correct hypo/hyperglycemia management
  • Teach the patient to carb counting
  • Teach the patient to calculate Sensitivity Factors for corrections, Carbs Ratio, Active insulin time, etc
  • Exercise activity and glucose changes
Reimbursement

- 95249 - CGM patient provided equipment, sensor placement, hook-up, calibration of monitor, patient training, and printout
- 95250 - CGM HCP (office) provided equipment, sensor placement, hook-up, calibration of monitor, patient training, removal of sensor, and printout
- 95251 - CGM analysis, interpretation and report
  - Can be billed monthly on ongoing basis
- General comments:
  - All codes require a minimum of 72 hours of data
  - Use -25 modifier for CGM codes if billing same day as a Problem Visit code (99212-99215) if significant an separately identifiable service took place
    - Ie 99212-99215: Pre-CGM evaluation (+) -25 95250: CGM start-up and instruction
CGM’S CURRENTLY AVAILABLE IN PR
Types of CGM

• Real Time CGM
  • CGM systems that measure glucose levels continuously and provide the user automated alarms and alerts at specific glucose levels and/or for changing glucose levels.

• Intermittent Scanning CGM
  • CGM systems that measure glucose levels continuously but only display glucose values when swiped by a reader or a smart phone that reveals the glucose levels

• Blinded (professional) CGM
  • CGM devices that measure glucose levels that are not displayed to the patient in real time. These devices are generally initiated in a clinic, using a reader that is owned by the clinic. They are removed after a period of time (generally 10–14 days) and analyzed by the patient and provider to assess glycemic patterns and trends
Abbot FreeStyle Libre

- Intermittent Scanning CGM
- Professional (Blinded) CGM available
- Factory Calibrated
- 14-day wear following 12-hr warm-up
- For best results need to read at least q8 hours
- No acetaminophen interference
User only gets a glucose reading when they wave the receiver device over the sensor which is unique to this CGM system.

The reader is 95mm x 60mm x 16mm and store up to 90 days of glucose readings.

Can be used with or without an insulin pump.

No calibration needed; pre-calibrated at the factory.

Lowest cost of any CGM on the market.

No automatic alerts for high/low glucose levels when user doesn't wave the receiver over the sensor.

14 day sensor, the longest lasting sensor in the CGM industry.
Freestyle Libre Report:

**Snapshot**
March 1, 2018 - March 14, 2018 (14 Days)

**Glucose**
- AVERAGE GLUCOSE: 141 mg/dl
  - % above target: 89%
  - % in target: 37%
  - % below target: 4%
- LOW GLUCOSE EVENTS: 3
  - Average duration: 40 min

**Sensor Usage**
- SENSOR DATA CAPTURED: 97%
  - Daily scans: 4

**LibreView**

**INSULIN**
- RAPID-ACTING INSULIN: 39.3 units/day
- Long-Acting Insulin: 25.9 units/day
- Total Daily Insulin: 66.3 units/day

**Comments**
- There was a ketone test. The result was 0.6 mmol.
- Gaps found in food data. 1 day in this reporting period has no recorded food events.
Dexcom G6

- Real Time, Stand Alone CGM
- No confirmatory fingersticks unless
  - Discrepancy with symptoms and readings
  - Device malfunction
- No Calibrations Needed
- Remote monitoring
- Alerts available
- 10 days sensor wear
Zero fingersticks: no calibration required, but can calibrate if sensor is off-track

FDA approved for ages 2+

Customizable high/low alerts

Readings may be viewed on a smart phone, smart watch (via phone Bluetooth connection), Tandem X2 insulin pump, or handheld receiver

Easy-to-use sensor applicator with one button insertion

Slim, water resistant sensor that lasts 10 days

2-hour warmup time for new sensor

* Smart phone and smart watch not included
Dexcom Clarity

Dexcom Clarity

7.0% 155 65

Enrique’s best glucose day was March 4, 2020.
Enrique’s glucose data was in the target range about 80% of the day.

This graph shows your data averaged over 14 days.

Above High Threshold
75th Percentile
Average
10th Percentile
Below Low Threshold

Periods with CGM data
100% 14/14
0.0

Sensor usage

Top Patterns

Mon Feb 24, 2020 - Sun Mar 8, 2020
Medtronic 670G

- Key unique features
  - First hybrid closed loop system
    - Modulates insulin infusion based on sensor glucose information
  - Predictive Low Glucose Suspend and Low Glucose Suspend
  - Calibration at least once every 12 hours (3-4x/day recommended)
  - 7 day sensor use
  - Acetaminophen sensitive
  - Approved for 14 years and older

Medtronic Guardian Connect

- Stand-alone CGM system
- Key unique features
  - No receiver; display device is iOS phone only
  - Predictive Alert Schedules
    - 10-60 minute prediction of hypo-/hyperglycemia based on threshold settings
  - Calibration at least once every 12 hours (4x/day recommended)
  - 7 day sensor
  - Acetaminophen sensitive
  - Approved for 18 and older
Calibration required 3-4 times daily

* Smart phone and smart watch not included

FDA approved for ages 14-75

Readings may be viewed on a smart phone or smart watch (via phone bluetooth connection)

Automatic upload to Carelink software

Customizable high/low alerts, including extended predictive alerts

Sensor life is 7 days

2-hour warmup time for new sensor
<table>
<thead>
<tr>
<th></th>
<th>Guardian Connect/640G SmartGuard</th>
<th>Dexcom G6</th>
<th>FreeStyle Libre</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensor life (days)</td>
<td>7</td>
<td>10</td>
<td>14</td>
</tr>
<tr>
<td>Alarms</td>
<td>Multiple</td>
<td>High, low and trend</td>
<td>None</td>
</tr>
<tr>
<td>Predictive</td>
<td>Yes</td>
<td>Yes</td>
<td>n/a</td>
</tr>
<tr>
<td>Trends</td>
<td>Yes</td>
<td>Yes</td>
<td>n/a</td>
</tr>
<tr>
<td>Rate change</td>
<td>Yes</td>
<td>Yes</td>
<td>n/a</td>
</tr>
<tr>
<td>Calibration</td>
<td>12-hourly</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>MARD</td>
<td>9.64%</td>
<td>9.0%</td>
<td>9.7%</td>
</tr>
</tbody>
</table>

Data taken from manufacturers’ specifications

*The manufacturer claims a sensor life up to 14 days; however, the device is only licensed for up to 7 days.

MARD = mean absolute relative difference.
CLINICAL EXAMPLES

Patients with DM 1-2 and Insulin Pump Therapy
CGM on non-diabetic patient
59 y/o F, BMI: 29 kg/m², HBP, no CGM

HBA1C: 7.2%
55 y/o F, BMI: 23.5 kg/m², HBP, no CGM

HBA1C: 7.8%
61 y/o F, BMI: 38 kg/m², HBP, Sensor Augmented Tx
HBA1C: 6.6%
56 y/o DM2 A1C 8.9% CAD, obesity, HBP, Dyslipidemia
61 F DM1 x 45 years: HbA1c: 11% – Happy to learn that will not perform finger sticks anymore!
There is no age limit for technology!!

- 82 y/o male
- Long standing DM2, low C-peptide
- On basal bolus
- Hx of recurrent severe hypoglycemia with 1-2 glucagon emergency kits per MONTH!
- rtCGM use, eliminated 100% hypoglycemia, A1C unchanged
THANKS!!