QUESTION 2. WHAT CGM DATA ARE RELEVANT AND HOW SHOULD THEY BE REPORTED?
Question 2a. What information from CGM technology is critical for patients and physicians to manage diabetes and improve outcomes?

- Identify patterns
  - Trend arrows toward hyper- and hypoglycemia
  - Recognize that BG fluctuations are a process in time characterized by BG value and rate/direction of change
- Hypo- and hyperglycemia alerts
- Meal-related glucose excursions
- Nighttime glucose patterns
- Modal day graphs that superimpose multiple days on the same plot are useful for detecting time of day patterns as well as hypo- and hyperglycemic periods and trends
- AGP is less useful because patients rarely keep consistent schedules for meals, snacks, exercise, work and sleep
- Accurate sensor data, especially for patients who use it for insulin dosing
- CGM traces in relation to insulin dosing, meals, and activity
- * Displays that combine pump data w/cgm data
- * Better algorithms to assist pattern recognition by treating clinician and patient
Q. 2Aa Cont. - Suggested Display and Report Information

Device Display for Real-Time Use

- Current glucose reading
- Direction and speed of change
- Values for the past three days at the same time

Download Report

- Graphic presentation of 1 to 5 days, with:
  - Mean at each time
  - Standard deviation
  - 95% confidence limit
  - Ability to stratify by weekday, weekend, day of week
  - Mean daily glucose over time

- Ambulatory glucose profile (Bergenstal 2013)

- Statistics (7,15,30 days):
  - Mean glucose by morning, noon, night
  - Mean daily glucose
  - Time in range (settable range)
  - Number of hypoglycemic episode, time in hypoglycemia
  - Glycemic variability, SD, COV, MAGE
  - Calculated A1c

See Notes view for citations
Question 2a. What information from CGM technology is critical for patients and physicians to manage diabetes and improve outcomes?

- Retrospective analysis of glucose trends and out of range alarm frequency can assist with treatment decisions; patients rely on alarms and graphs to act on results
- Patient should have access to same info as physician
- Passive – not manual collection of data – on multiple inputs: diet, sleep, step – and become actionable
- Capturing info from pens and insulin pumps
- Measures that would facilitate increased time in range, rather than emphasize extremes in blood glucose
- Frequency of hypoglycemia, alerts, and predictions of low BG
- Raw data should be available but presented in a way that enables patients to comprehend it and take action
- Data downloads that show the impact of insulin and behavior (exercise, food choices, etc) on blood sugar
- A negative impact of CGM is that patients can be more cavalier about hypoglycemia, with over-reliance on CGM alarms, etc
- Modal day and hourly trend data are crucial, along with estimated A1c with statistics that include hourly and overall averages, SD, max, min, etc. Having the data graphed out in an easy to visualize manner is also important
Question 2a. What information from CGM technology is critical for patients and physicians to manage diabetes and improve outcomes?

- Real-time glucose concentration
- Glucose trends, to help avoid hypo- and hyperglycemia
  - Need better algorithms for trend analysis to enhance prediction of future hypoglycemia episodes and better tailor insulin therapy
- Adherence data
- Recording of meals and meal boluses, activity, alcohol, stress, etc
- *Medications
- *Illness
Question 2a. What information from CGM technology is critical for patients and physicians to manage diabetes and improve outcomes?

- Patient use needs to be individualized
  - Intermittent vs Continuous use
  - Alarms (vs no alarms)
    - Default values
    - Trends are very important
- Clinicians need to be able to track patterns of hypoglycemia, hyperglycemia, and glycemic variability
- CGM data should be put in context with other system variables such as meals, treatments, exercise, illness, boluses, and AP algorithm activity
- Pattern recognition software that identifies the highest risk patterns could facilitate interpretation/utilization by HCPs ("ECG-like")
- Ease of downloading is CRITICAL
Q. 2a Cont. - Suggested Recommendations for Reporting of CGM Data

<table>
<thead>
<tr>
<th>Clinical Need Statement</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Real time glucose, trend arrow, and graph of recent glucose readings</td>
<td>Standard data/reporting for personal CGM</td>
</tr>
<tr>
<td>Visualization of the glycemic pattern at each hour of the day to understand overall</td>
<td>Ambulatory Glucose Profile (hourly lines of 10th, 25th, 50th, 75th and 90th</td>
</tr>
<tr>
<td>glycemic control</td>
<td>percentiles) over a 24 hour (midnight to midnight) period</td>
</tr>
<tr>
<td>Metrics to assess glucose control and track progress for:</td>
<td></td>
</tr>
<tr>
<td>• Hypoglycemia</td>
<td>Hypoglycemia:</td>
</tr>
<tr>
<td>• Hyperglycemia</td>
<td>1. Time below 70 mg/dL (minutes/day)</td>
</tr>
<tr>
<td>• Glycemic Variability</td>
<td>2. Time below 55 mg/dL (minutes/day)</td>
</tr>
<tr>
<td></td>
<td>3. Time below 45 mg/dL (minutes/day)</td>
</tr>
<tr>
<td></td>
<td>Hyperglycemia: eA1c (estimated A1c)</td>
</tr>
<tr>
<td></td>
<td>Glycemic Variability: IQR (interquartile range)</td>
</tr>
<tr>
<td></td>
<td>Additional: % time below, within, above Target Range</td>
</tr>
<tr>
<td>Assess specific glycemic episodes.</td>
<td>Daily glucose traces annotated with available contextual information (food, insulin, exercise, etc.)</td>
</tr>
</tbody>
</table>
Question 2b. What key metrics should be considered: time in range, percent time above/below range, etc.?

• Time in target range
• Time in hypo- and hyperglycemia
• Time above/below target range
• SD (glycemic variability)
• MAGE
• CV
• Mean/average BG

• % time in target range
• % in hypo- or hyperglycemia
• Calibration frequency
• Calculated A1C
• Glycemic trending
• Point accuracy
• Composite hypoglycemic score
• High and Low BG Index
Q. 2b Cont. - Numerical Measures Based on BG Data

<table>
<thead>
<tr>
<th>Average Glycemia and Deviations from Target</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean BG</td>
</tr>
<tr>
<td>Mean pre-meal BG</td>
</tr>
<tr>
<td>Mean post-meal BG</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Deviations from Target</th>
</tr>
</thead>
<tbody>
<tr>
<td>% time spent within target range of 70-180 mg/dl; time below 70; above 180 mg/dl</td>
</tr>
<tr>
<td>% time &lt;= 50 mg/dl</td>
</tr>
<tr>
<td>% time &gt; 300 mg/dl</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Variability and Risk Assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inter-Quartile Range</td>
</tr>
<tr>
<td>Low BG Index (LBGI)</td>
</tr>
<tr>
<td>High BG Index (HBGI)</td>
</tr>
<tr>
<td>SD of BG Rate of Change</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Events and Other Clinical Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Events of low BG &lt; 70 mg/dl (or events of BGs &lt; 50 mg/dl);</td>
</tr>
<tr>
<td>Events of high BG &gt; 180 mg/dl (or BGs &gt; 300 mg/dl);</td>
</tr>
</tbody>
</table>
## Q. 2b Cont. - Graphs Visualizing CGM Data

<table>
<thead>
<tr>
<th><strong>Average Glycemia and Deviations from Target</strong></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose trace</td>
<td>Traditional plot of frequently sample glucose data;</td>
</tr>
<tr>
<td>Aggregated glucose trace</td>
<td>Correlates to time spent below/within/above a preset target range. Visualizes the crossing of glycemic thresholds;</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Variability and Risk Assessment</strong></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk trace</td>
<td>Corresponds to LBGI and HBGI. Designed to equalize the size of glucose deviations towards hypo- and hyperglycemia, emphasize large glucose excursions, and suppress fluctuation within target range, thereby highlighting essential variance;</td>
</tr>
<tr>
<td>Histogram of BG Rate of Change</td>
<td>Represents the spread and range of glucose transitions. Related to system stability. Corresponds to SD of BG Rate of Change;</td>
</tr>
<tr>
<td>Poincaré plot</td>
<td>The spread of the data indicates system (patient) stability – more widespread data points are associated with unstable diabetes and rapid glucose fluctuations.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Event-Based Clinical Characteristics</strong></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Control Variability Grid Analysis</td>
<td>Represents the effectiveness of glycemic control at a group level. Corresponds to event-based characteristics.</td>
</tr>
</tbody>
</table>

Question 2b. What key metrics should be considered: time in range, percent time above/below range, etc.?

- Time in range
  - Day
  - Night
  - Below (especially below 55)
  - Above
- MAGE and SD
- Setting individualized targets
- Glycations gaps

- Percentage time above and below range
- Comparisons between CGM, SMBG, and insulin dose to identify deviations from regimen
- Rate of change

- Metrics need to be displayed and/or communicated in patient-friendly manner
- There should be at least 2 layers of information organized in an easy to view/understand manner. The second layer could be more sophisticated to dig deeper into the information

MAGE = mean amplitude of glycemic excursions
Question 2b. What key metrics should be considered: time in range, percent time above/below range, etc.?

• Time in range
  – Day
  – Night

• Time above and below thresholds for hypoglycemia and hyperglycemia
  – Measure of more severe out of range levels

• Glucose variability and correlation with A1C

• Important for stakeholders to agree on definitions of each metric

• Data readouts
Question 2b. What key metrics should be considered: time in range, percent time above/below range, etc.?

- Time in range
- % time >180 mg/dL
- Hyperglycemia standardized on estimated A1C metric
- % time <70 mg/dL
- % time <55 mg/dL
- % time <45 mg/dL
- Glycemic variability standardized on interquartile range
- Average (mean) CGM
- Standard deviation (SD) of CGM
- AGP
Question 2b. What key metrics should be considered: time in range, percent time above/below range, etc.?

Cont.

• TIR
• AUC above range – call hyperglycemic exposure/burden
• AUC below range – call hypoglycemic exposure/burden
• Average/mean glucose
• Time above/below target
• eA1C – thought to be difficult from regulatory standpoint
• frequency or severity of hypoglycemia (risk)
Question 2c. Would standardized reporting support patient management, physician utilization, and training of physicians and patients?

Yes

• Reporting variations discourage HCPs from learning to use CGM
• Standardized reporting and analysis would help clinicians
  – Develop expertise in CGM use
  – Enhance quality of care through enhanced pattern recognition
  – Improve practice efficiencies
  – Engage patients, thereby reinforcing consistent use of CGM technology
• The basic report should be standardized
• * In pump patients, basal and bolus insulin doses overlaid with CGM

Challenges

• Variability in individual data
  – In injection patients, missed doses unaccounted for
  – Many other factors not accounted for, including lack of carb counting skills, exercise, stress management, etc.
Question 2c. Would standardized reporting support patient management, physician utilization, and training of physicians and patients?

Yes

- Standardized reporting would help physicians, patients, and the healthcare system
  - Must overcome perception of CGM manufacturers that their software offers competitive advantages
  - Standardization would help achieve data and device interoperability
  - Patient and provider education are key to success
  - * Data should be same for patient and physician—transparency phys & patient

No

- Dataset standardization is more pressing than report standardization; reports should be customizable for the HCP to provide individualized support
  - Standardized data reporting would be useful but it’s limited by variations in glucose reading accuracy among different devices
  - Standardized data are of lesser importance than communication, interpretations, and recommendations to the patient
Question 2c. Would standardized reporting support patient management, physician utilization, and training of physicians and patients?

• Yes

• More uniform reporting optimizes patient care.
Question 2c. Would standardized reporting support patient management, physician utilization, and training of physicians and patients?  **YES**

- Standardized homepages (with customizable features) for reporting basic information should be instituted on all devices—this would support CGM adoption

- Standardization of software will not hamper innovation. Marketing departments, listen up...
Question 2d. What data are necessary? How should they be standardized (eg, should data be broken into different times such as fasting, postprandial, bedtime, hypoglycemic episodes and their times)?

- Software to identify most prominent patterns of hyper- and hypoglycemia, prioritizing nocturnal → daytime → overcorrection from high to low BG
- Modal day reports that begin at time meals are consumed (ie, time at which meal bolus is delivered), with ability to sort data by days of the week and display trend data following specific events such as exercise and infusion set changes
- Daily trend overlays
- Ambulatory glucose profile of past week with mean and hypoglycemic episodes highlighted
- Statistics showing time in range, glucose exposure, glycemic variability (SD, CV, or IQR), number and duration of hypoglycemic episodes, hyperglycemia, calculated A1C
- * One size doesn’t fit all
- * More seamless integration of data to facilitate interpretation with clinician and patients
Q. 2d Cont. - Glucose Target Ranges and Categories

Glucose Target Ranges and Categories

<table>
<thead>
<tr>
<th>Plasma glucose (mg/dl)</th>
<th>Glucose categories</th>
</tr>
</thead>
<tbody>
<tr>
<td>400</td>
<td>Dangerously High</td>
</tr>
<tr>
<td></td>
<td>22.2</td>
</tr>
<tr>
<td>250</td>
<td>Very High</td>
</tr>
<tr>
<td></td>
<td>13.9</td>
</tr>
<tr>
<td>180</td>
<td>High</td>
</tr>
<tr>
<td></td>
<td>10.0</td>
</tr>
<tr>
<td>70</td>
<td>In Range</td>
</tr>
<tr>
<td>60</td>
<td>Low</td>
</tr>
<tr>
<td>50</td>
<td>Very Low</td>
</tr>
<tr>
<td>0</td>
<td>Dangerously Low</td>
</tr>
</tbody>
</table>

Glucose related clinical diagnoses & safety measures

Increasing risk for DKA
- Metabolic acidosis
- Ketonemia
- Hyperglycemia

Increasing risk for severe hypoglycemia
- Assistance required
- Major severe hypoglycemia
- Medical personnel assistance required (ambulance, ER, hospital)
- Seizure, coma, death

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Question 2d. What data are necessary? How should they be standardized (eg, should data be broken into different times such as fasting, postprandial, bedtime, hypoglycemic episodes and their times)?

- All metrics listed in Q2b are necessary but modal day, hourly trends, SD should be displayed on top
  - Users need to be able to define times of activity (fasting, sleeping, eating, exercising)
- Industry should recognize that fasting, postprandial, bedtime, activity times, etc, are not fixed times
- Data collection should minimize manual action by user. Each time the user must enter data manually increases user burden
- Data should be organized by event, time of day, and trends, and data collected should include percentage of time above and below targets, hypoglycemia and hyperglycemia, changes in patient weight, onset of DM complications
- * Real-world data with HEOR
Question 2d. What data are necessary? How should they be standardized (e.g., should data be broken into different times such as fasting, postprandial, bedtime, hypoglycemic episodes and their times)?

- In addition to blood glucose metrics (see Q2b), data on illnesses and activities should be considered.
- Data collection may need to be individualized based on patient’s metabolic profile.
- Data collection in clinical studies will depend on study endpoints established in protocol.
Question 2d. What data are necessary? How should they be standardized (e.g., should data be broken into different times such as fasting, postprandial, bedtime, hypoglycemic episodes and their times)?

• Already discussed.
• At issue is what format is chosen.
  – Consensus group (Bergenstal 2013) had recommended customized AGP
  – This has only been adopted by 1 company to date

• Is critical for medical office staff training
Question 2e. Can unnecessary data distract from key findings? If so, should a series of algorithms be developed to assist with a focused and meaningful analysis and interpretation?

**Yes**

- Need to develop standardized algorithm focusing on prioritizing nocturnal hypo → daytime hypo → overcorrection from high to low BG
- Estimated A1C distracts from more important data such as % time in hypoglycemia
- Whisker graphs hard to read and interpret
- Pie charts useful
- Hypoglycemia risk is useful
- IDC has developed a data analysis software program that highlights key data
- * Streamline data to make more pertinent and usable by and for the patient

**No**

- No Response
Q. 2e – Cont. - The AGP Dashboard
Question 2e. Can unnecessary data distract from key findings? If so, should a series of algorithms be developed to assist with a focused and meaningful analysis and interpretation?

**Yes**
- Simplified standard reports are most important, with the ability to customize data downloads to fit particular needs
- Stakeholders should reach consensus on identifying a small number of most-useful analytic charts (but everyone will have their own preferences)
  - A “dashboard” of reports for HCPs and patients (eg, glucose trends by day, hypoglycemia periods, etc)
  - * More of a physician issue
  - * simplified reporting/dashboard

**No**
- Since each patient’s DM experience varies, individuals should be able to customize reports to suit their needs
- All data points should be accessible to patients and HCPs, although smart algorithms are needed to identify the most meaningful data
- The patient and HCP should decide which data are important for each patient
- While “unnecessary” data can be distracting, it’s uncertain which CGM data are “unnecessary”
Question 2e. Can unnecessary data distract from key findings? If so, should a series of algorithms be developed to assist with a focused and meaningful analysis and interpretation?

- Yes. Personalized algorithms may be needed for proper assessment of benefits
- -- Different literacy levels of report customized on patient’s needs
- -- level of understanding
Question 2e. Can unnecessary data distract from key findings? If so, should a series of algorithms be developed to assist with a focused and meaningful analysis and interpretation?

• Experienced clinicians will not have a problems
• Filters / algorithms to ease interpretation will be helpful, and likely will be company/device – specific.
Question 2e. Can unnecessary data distract from key findings? If so, should a series of algorithms be developed to assist with a focused and meaningful analysis and interpretation? Cont.

- Because clinicians need to be able to individualize care to each patient, all information should be made available. However, data management software that presents a simple “home page” that includes basic glucose information in combination with pattern recognition/decision support would facilitate more widespread use of CGM. Interpretation of results should be prioritized based on clinical need (e.g., nocturnal hypoglycemia).

- Event recording capability is necessary to help clinicians interpret patterns

- Default reports should be customizable by the HCP, so he/she can determine which data to show, but all relevant parameters should be retrievable