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CLINICAL APPLICATIONS

Optimizing Display, Analysis, Interpretation and Utility of Self-Monitoring of Blood Glucose (SMBG) Data for Management of Patients with Diabetes

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Abstract

Background:

Self-monitoring of blood glucose (SMBG) data have not been used to fullest advantage. Few physicians routinely download data from memory-equipped glucose meters and perform systematic analyses and interpretation of the data. There is need for improved methods for display and analysis of SMBG data, for a systematic approach for identification and prioritization of clinical problems revealed by SMBG, for characterization of blood glucose variability, and for clinical decision support.

Methods:

We have developed a systematic approach to the analysis and interpretation of SMBG data to assist in the management of patients with diabetes. This approach utilizes the following criteria: 1) Overall quality of glycemic control; 2) Hypoglycemia (frequency, severity, timing); 3) Hyperglycemia; 4) Variability; 5) Pattern analysis; and 6) Adequacy of monitoring. The "Pattern analysis" includes assessment of: trends by date and by time of day; relationship of blood glucose to meals; post-prandial excursions; the effects of day of the week, and interactions between time of day and day of the week.

Results:

The asymmetrical distribution of blood glucose values makes it difficult to interpret the mean and standard deviation. Use of the median (50th percentile) and Inter-Quartile Range (IQR) overcomes these difficulties: IQR is the difference between the 75th and 25th percentiles. SMBG data can be used to predict the A1c level and indices of the risks of hyperglycemia and hypoglycemia.

Conclusion:

Given reliable measures of glucose variability, one can apply a strategy to progressively reduce glucose variability and then increase the intensity of therapy so as to reduce median blood glucose and hence A1c, while minimizing the risk of hypoglycemia.

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Abbreviations: (ADRR) average daily risk range, (CV) coefficient of variation, (FOM) figure of merit, (HBGI) high blood glucose index, (IQR) inter-quartile range, (LBGI) low blood glucose index, (MAGE) mean amplitude of glycemic excursion, (MODD) mean of daily differences, (PCP) primary care physician, (SD) standard deviation, (SMBG) self monitoring of blood glucose

Keywords: clinical decision support, diabetes, glucose, medical informatics, self-monitoring, statistics, variability

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Introduction

The Problem

Increasing the frequency of self monitoring of blood glucose (SMBG) has been associated with improvement in the quality of glycemic control in patients with diabetes.[1-3] SMBG data are typically used by patients to detect or confirm hypo- or hyperglycemia and to take corrective actions in terms of self-adjustment of insulin dosage and timing, adjustments of other medications, or adjustment of the amount, content, and timing of meals. Retrospective analysis of SMBG data is typically performed by inspection of logbook data at the time of ambulatory care visits. Glucose meters equipped with memory and ancillary software for downloading and analysis of these data have been available for more than 20 years. However, downloading data from memory meters and computer analysis of SMBG data is used by only a small fraction of physicians caring for patients with diabetes and for a tiny fraction of patient-physician encounters.

In addition to tabulating the data and providing graphical and statistical analysis, the computer can provide a clinical decision support system using an *artificial intelligence* or rule-based expert system to identify and prioritize the most important problems facing the patient. The basic principles underlying such approaches have been defined previously.[4-11]

The present report examines:

a) recent developments that suggest a growing need for computer analysis and clinical decision support;

b) barriers to implementation of these kinds of approaches;

c) some approaches to overcoming those barriers;

d) a systematic approach to the analysis of SMBG data that can be used by primary care physicians (PCP); and

e) improved methods for display, analysis, interpretation and application of SMBG data.

The current state of the art

Hirsch,[12-14] Monnier,[15] and others[16-19] have emphasized the evidence suggesting the importance of blood glucose variability in generating oxidative stress and potentially contributing to the development of both macro- and micro-vascular complications of diabetes. Recently Kilpatrick[20] performed a retrospective analysis of DCCT data, and reported that variability plays only a very small role relative to the average level of blood glucose as reflected in A1c. However, this may be due to the fact that there is a very high correlation between mean level and variability, so that failure to find a strong effect for variability per se may be due to the *co-linearity* of mean and standard deviation (D. Rodbard, unpublished observations). Only by means of computer analysis can we obtain objective measures of variability. Accordingly, use of frequent SMBG measurements, memory meters, downloading of data and computer analysis have assumed increasing importance. There is a need to reexamine the multiple options for measurement of blood glucose variability.

Numerous systems have been developed to provide computer analysis and display of capillary blood glucose data. Some systems will also permit data entry for other information, (e.g. records of insulin and other medications, diet, exercise, illness, "meal markers," and comments), so that the meter can also provide the functionality of the traditional pen and paper logbook. Such electronic logbooks have been shown to improve the quality of glycemic control in randomized and observational studies.[21] Currently available programs provide a series of graphs and statistics, and analyses by date, time of day, relationship to meals, day of week, a tabular logbook display and a variety of ancillary information. Some patients use spreadsheet, word processing and database software to store and analyze their data. However, these kinds of analysis are not yet the *standard of practice* for diabetes care in the majority of clinics and offices. The potential benefits of these systems have yet to be fully realized.

Barriers to Use of Downloading and Analysis of Memory Glucose Meters

Some physicians erroneously believe that it is not necessary to analyze SMBG data in detail because the laboratory measurement of A1c provides an adequate basis for assessing the quality of glycemic control. Patients may not have access to the memory meter, computer, or software and often fail to bring their memory-equipped meters to the clinic. Physicians usually do not have the time required to download a meter themselves. Likewise, physician office staff members usually do not have the time and other resources to download the data and generate a report for the physician. For practical purposes, at present, there is little or no remuneration for these services.

Another barrier may be that the analyses and reports provided by the software are not sufficiently informative, useful and relevant to the clinical management decisions which the busy clinician must make at the office visit.

Improved methods of analysis

Customization

There is a need for customization of the methods of display and analysis. The analysis for a patient with Type 2 diabetes on oral anti-diabetic agents and testing glucose twice per day is usually very different from that for a patient with Type 1 diabetes receiving intensive insulin therapy and testing 4 to 6 times per day. Primary care physicians may have different requirements and time constraints than endocrinologists. Customization may be desirable for each patient. Clinics, institutions, and health care systems may wish to utilize their own criteria or *norms* for interpretation of results and for thresholds to trigger reminders and alerts. Hence, there is the need for a high degree of customization.

Making provision for customization results in an increased burden for the end user who must learn how to select the options and set the parameters. It would be desirable to identify and train one person at each clinic to customize the software for use by other health care providers.

Standardization

Customization has a downside. It means that reports will vary from patient to patient and from one visit to another, depending on the particular meter, software or options that are used on a particular day. Further, the customization of a large number of parameters requires training to learn the options and time for data entry. To minimize confusion and the risk of misinterpretation, there is a major advantage to using standardized reports, where graphs are presented on the same scales, in the same order, with the same color coding, symbols, and with the same logic for detection and interpretation of patterns. Clearly, there is need for a *trade-off* between customization and standardization, which needs to be resolved by the end user.

Graphical displays

Almost all software applications for analysis of blood glucose data employ a variety of graphical displays. Most of these have not been evaluated in terms of their effectiveness, usability, and user-friendliness.

Tabular displays

There are a wide variety of options for tabular displays of data. There are a series of trade-offs between simplicity and level of detail.

A number of questions arise:

1. To what extent should one display results that are partially redundant (e.g. mean and median, or standard deviation and IQR)?
2. Which of the many statistics should one display? (Examples: Maximum, minimum, number of observations, median, mean, Inter-Quartile Range, 25th percentile, 75th percentiles, standard deviation, percentage of values below, within, or above the target range, standard error of the median, standard error of the mean, 95 percent confidence intervals for mean.)
3. Which aspects of the report should be customizable?

Measures of central tendency (Median, Mean) and variability (Inter-Quartile Range and Standard Deviation)

Mean

Most of the commercially available programs for analysis of SMBG data have used the mean and standard deviation (SD) as measures of *central tendency* (average) and variability, respectively. However, glucose values from SMBG do not follow a *Gaussian or normal* distribution. Instead, the distribution is usually *skewed to the right*. For a symmetrical Gaussian distribution, the range between (mean - 1 SD) and (mean + 1 SD) will encompass 68% of the data points and the range between (mean - 2 SD) and (mean + 2 SD) will encompass about 95% of the observations. However, these relationships do not apply to a skewed distribution.

There are two significant problems with use of the arithmetic mean: the mean can be easily perturbed by even a single *outlier* or aberrant value. Also, glucose meters have a discrete range of measurement. If a value is outside of this range, it will be recorded as *High* or *Low,* creating ambiguity with regard to the calculation of the mean.

Median: We recommend the use of the median (the 50th percentile) in lieu of the mean. The median has several advantages: it is very *insensitive* to outliers, and is essentially *unaffected* by values that are outside the range of measurement of the meter. The median has another important advantage: the physician can explain it to the patient very simply as: "Half your glucose values are above

the median and 50% of your glucose values are below the median. The median is the middle value and serves as a kind of average."

However, the median does have two drawbacks:

1) The median is less familiar to most people than the simple arithmetic average; and

2) The median is subject to somewhat larger sampling error (random variation in measurement) than the mean. The standard error of the median is approximately 1.23 fold larger than the standard error of the mean. This is an *asymptotic* result when dealing with a large number of observations and with an underlying Gaussian distribution. Thus, the mean is a more efficient measure of central tendency *if all of the assumptions are satisfied*.

Accordingly, to obtain the same precision of measurement of the median as for the mean, we would need a larger number of measurements.

Values for the median are highly correlated with those for the mean. We expect that the correlation between the median blood glucose and the A1c values would be just about as close as mean blood glucose and the A1c.

Standard deviation: The usual *sample standard deviation* (SD) is readily perturbed by a single outlier or by values that are outside the range of measurement for the meter. Most users are not sufficiently familiar with the concept of the standard deviation, and cannot describe how it is calculated or how to interpret it. One can inform the patient that the SD is a *measure or index of variability*. However, it is likely to remain a vague, abstract concept.

Range: One could potentially characterize the variability of the distribution in terms of the range, that is, the difference between the highest (maximum) value and the lowest (minimum) value. However, the range has two serious problems: 1) the range is even more sensitive to a single aberrant value or "outlier" than the standard deviation, and 2) the expected value of the range depends on the number of observations. Therefore, if we have 50 measurements, we would expect to have a larger range than if we have only 10 measurements, since the range is, by definition, completely determined by the highest and lowest values.

Inter-Quartile Range: To avoid the problems with the Range, it is desirable to use the Inter-Quartile Range (IQR). The IQR is the difference between the 75th percentile and the 25th percentile, i.e., the difference between the upper limits of the 3rd quartile and 1st quartile. By definition, 50% of the glucose measurements fall within the IQR, since 25% of the values fall below the 25th percentile, and 25% fall above the 75th percentile. The IQR may be less familiar than the standard deviation, but it is very popular in *exploratory data analysis* which was designed to handle data that depart from a normal or Gaussian distribution.[36] The IQR does not depend on the largest and smallest values. Accordingly, it is very insensitive to one or two or even a few outliers. Similarly, the IQR is unaffected by values above or below the range of measurement for the meter.

Relationship of the IQR to the standard deviation: If the distribution were symmetrical and normal or Gaussian, then one can compute the relationship between the expected value of the IQR and the expected value of the standard deviation.

$$IQR = 1.35 \times SD \qquad \text{(Equation i a)}$$

Using this relationship, we can compute an apparent or effective standard deviation, SD', from the IQR:

$$SD' = IQR/1.35 \qquad \text{(Equation i b).}$$

Thus, by obtaining the IQR, we can obtain a robust estimate of the SD that is insensitive to the presence of outliers or values outside the measurement range of the meter. Accordingly, people who are accustomed to thinking in terms of the SD can easily convert the IQR into an approximate measure of SD.

When showing graphical displays of glucose by date, glucose by time of day, glucose in relationship to meals, or glucose by day of the week, it is desirable to show the median, the 25th percentile, and 75th percentiles superimposed on the data points representing the original measurements This type of display is usually more readily understandable than a histogram or frequency distribution, which are unfamiliar to most patients and which lose the information regarding individual observations.[5,6] The 25th and 75th percentiles will be applicable and readily understandable irrespective of the degree of asymmetry of the distribution. These kinds of graphical displays have the advantage that they retain the individual data points while characterizing the distribution. The maximum and minimum values of the distribution are also readily apparent. When dealing with a small number of observations, the IQR can be unstable due to *random sampling variability*, (i.e., subject to random variability depending on the particular data points that are included). Accordingly, it is sometimes desirable to use curve smoothing for the median, 25th and 75th percentiles. If there are only a very small number of observations such that the random sampling error is large and the percentiles are unstable, then display of these percentiles can and should be suppressed.

Other methods to characterize variability

Several other methods can be utilized to provide indices of variability.

Coefficient of Variation (CV): The coefficient of variation (CV or %CV) is defined as the ratio of the standard deviation to the mean, expressed as a percentage:

$$\% \text{ CV} = 100 \times \text{SD}/\text{Mean} \qquad \text{(Equation ii)}$$

Therefore, we can speak of a 33% CV or a 50% CV. Hirsch has suggested that good control of blood glucose should be accompanied by no greater than a 50% CV, i.e., SD < 0.5 x Mean, and that, preferably, one should have no greater than a 33% CV (SD < 0.33 x Mean).[12] However, the acceptable or allowable range for the IQR, SD and %CV will vary systematically with the average or median value of the blood glucose.

LBGI, HBGI, ADRR: Kovatchev has utilized transformations of the glucose values to obtain a variable with a distribution that is very nearly symmetrical. He then developed two indices, the *Low Blood Glucose Index* (LBGI) and the *High Blood Glucose Index* (HBGI).[22-25] The LBGI has been validated as a predictor of the frequency with which subjects experienced hypoglycemia during a subsequent six month period. Recently, Otto, *et al.* have utilized a combination of the LBGI and HBGI as an overall index of variability, designated as the Average Daily Risk Range (ADRR).[25] The ADRR is one of several available indices of overall quality of glycemic control, and appears to be the best predictor of the frequency of glucose values being *out of range* (e.g. below 70 or above 180 mg/dL).

Other Indices of Overall Quality of Glycemic Control (M-value, MAGE, MODD, J-index, Figure of Merit): Several authors have developed methods that attempt to provide an overall index of glycemic control. These measures (including ADRR) are sensitive to variability. These indices include the Schlichtkrull M-value,[26] Mean Amplitude of Glycemic Excursion (MAGE),[27,28] Mean of Daily Differences (MODD),[27,28] J-index,[29] and a recently described *Figure of Merit (FOM)*.[30]

Interpretation of measures of blood glucose variability

We would like to be able to convert any value for the IQR into a *score* or simple qualitative category of the degree of variability. One might like to be able to tell the patient: "The variability in your blood glucose values is 'Excellent' (or alternatively, 'Good,' 'Fair,' 'Poor,' or 'Excessively large'). This involves a subjective judgment. The best approach could be to interpret the value with reference to a database of *normative data*. We would need to define a reference population, for example, all patients, with the same type and duration of diabetes, being treated at the same facility (possibly by the same physician or group of physicians), and receiving the same therapeutic regimen. Once the normative population has been defined, then we might regard the smallest 20% of the IQRs as Excellent; the next 20% as Good; the next 20% as Fair; the next 20% as Poor; and finally, the highest 20% or quintile as Unacceptable. In order to interpret measures of variability (whether this be a IQR, SD, %CV, or ADRR) in this manner, one must collect data on a large number of subjects.

It would also be helpful to establish criteria for Excellent, Good, Fair, Poor for IQR and SD depending upon the average value (median or mean) for the blood glucose values. An IQR of 50 mg/dL would pose dramatically different risks for hypoglycemia depending on whether the median glucose level is 175, 125 or 110 mg/dL. Assessment of hypoglycemia or hyperglycemia risks (e.g., with the ADRR (25)) may help define the qualitative scoring for IQR as a function of median glucose level.

Some physicians may prefer to evaluate variability simply in terms of the percent of glucose values in target range; the percent *very high*, the percent *high*, the percent *low* and the percent *very low*. The definitions of these ranges will depend on the choice of target range and may depend on time of day.

Another important approach to evaluate variability is to examine the graphs of glucose versus date, glucose versus time of day, glucose versus meal times, and glucose versus day of week. These require the downloading of the meters and automatic generation of graphical displays, since it is not practical to create these graphical displays manually. It is desirable to show the target range, the median, 25th and 75th percentiles, and IQR for local segments of the data.

Glucose Pattern Analysis

We have developed a systematic approach to the analysis of SMBG data that should be broadly applicable (**Table 1**). Clinicians may seek to systematically address a series of questions such as these for each patient at each visit in order to identify potential problems. The exact order and wording of the questions is arbitrary, but each of these constructs or concepts should be addressed.

Table 1. A Systematic Approach to Analysis of SMBG Data

1. Are there **sufficient data** available to perform an analysis?
   a) What is the adequacy of the frequency of SMBG monitoring, relative to goals set by the physician?
   b) At what times of day (and what relationships to meals), and on what days of the week, would it be desirable to obtain a higher frequency of SMBG values?

2. What are the **major problems** that need to be addressed?
   e.g., Hypoglycemia before lunch (or other specified mealtime or time of day)
   Hyperglycemia after dinner (or other specified mealtime or time of day)
   Excessive post-prandial excursions
   Systematic trend upward/downward overnight
   Is there evidence of "rebound," (i.e., hypoglycemic events followed shortly thereafter by hyperglycemia, due to the counter-regulatory hormone response or due to over-treatment with rapidly absorbed carbohydrate)?
   Is there evidence of "over-correction" or of "under-correction" in response to hyperglycemic events, (i.e., hyperglycemic values followed within a specified time by hypoglycemic events)?

3. **Is the overall level of control viewed in terms of SMBG consistent with the measured value of A1c?**
   Is the value of A1c predicted from the SMBG data consistent with the reported A1c, within the limits of error? (24,31-32) Any major discrepancy may deserve follow up

4. What is the overall measure of "quality of glycemic control"?
   Average (median) **level:** Is the patient ***"at goal" in terms of average (median) glucose?***
   Variability
   Inter-Quartile Range (IQR) (5,6)
   Standard Deviation (SD)
   % very low, % low, % in target range; % high, % very high
   Other indices: ADRR (22-25), "Figure of Merit (FOM)" (30), M-value (27,28), J-index (29)
   How does this patient compare with other patients in an appropriately chosen reference population (e.g., patients with the same type of diabetes, of approximately the same duration, seen at the same treatment facility/clinic during the same period of time, receiving a similar kind of treatment)?

5. How does glycemic control vary with **date, time of day, and day of the week?**
   a) **Glucose by Date:** How do the current results for the patient compare with results on previous downloads?
      Is there a **significant trend of glucose values longitudinally with date?** If so, is it linear or nonlinear? What is the best way to describe it?
      Are any temporal changes in glycemic control correlated with changes in lifestyle, medication dosage, or treatment regimen?
      Are the **data** for a given period of time **sufficiently stable** to permit pooling of data to analyze glucose by time of day, in relationship to meals, and by day of the week

   b) **Glucose by Time of day:**
      Is there significant variation of glucose in relationship to meals? What is the typical or "average" post prandial excursion for each of the major meals and snacks, and for all meals combined?
      Are there systematic trends in glucose during the day and night (e.g., an upward trend during the day and downward trend at night, or vice versa)?

   c) **Glucose by Day of Week:**
      Is there a significant relationship between **glucose and day of the week**?
      Is there a significant **"interaction" between time of day and day of the week**?

Table 1. An example of a systematic approach to the analysis and interpretation of SMBG data based on downloads of a memory meter with use of appropriate software so as to identify potential problems.

Identification of Potential Clinical Problems

The initial analysis of blood glucose data is to identify potential problems (e.g., overall level of control, hypoglycemia, hyperglycemia, variability, adequacy of monitoring) and relate those to time of day, day of the week and other factors. In most cases this is likely to result in a lengthy list of potential problems, often more than can be addressed in a single outpatient office visit.

The next step is to *prioritize* the problems. The rules for doing so may vary from physician to physician, and depend on the nature of the patient's condition (type of diabetes, duration of diabetes, type of therapy, co-morbidities, complications, etc.). **Table 2** provides one example of a systematic approach to prioritization of potential problems.

Table 2. Prioritization of Potential Clinical Problems

1. Hypoglycemia
Overnight (nocturnal)
Bedtime and fasting (before breakfast)
Other preprandial glucose values
Postprandial glucose values
2. Hyperglycemia
Fasting
Other preprandial glucose values
Postprandial glucose values
3. Variability
Co-occurrence of hypo- and hyperglycemia at a specified time of day, or in association with a specified "meal time" (e.g. "Before Dinner")
Variability associated with a particular time of day or in association with a specified "meal time"
Variability by date
Variability by day of week
Interaction of the effects on glucose related to time of day (or meal times) by day of week.
Variability in timing of meals
4. Patterns
Postprandial excursions
Daytime - nighttime variability
Evidence of hypoglycemia followed by rebound
Evidence of hyperglycemia followed by excessive or inadequate corrections
Dawn phenomenon (elevation of blood glucose in the 5 AM - 7 AM timeframe)
5. Overall level of control
Actual A1c and trends in A1c
A1c predicted on the basis of the SMBG data (24,31,32)
Median, % in Target range
Combined Indices of overall level of control
ADRR, "Figure of Merit," Schlichtkrull M-value, J-index, MAGE (23-29)
6. Adequacy of self monitoring of blood glucose (SMBG)
Preprandial
Postprandial
Bedtime
Overnight
By day of week

Table 2. An example of a systematic approach to prioritizing potential clinical problems identified by the "Pattern Analysis."

After the data have been analyzed with regard to the issues identified in **Table 1** and the potential problems have been *identified*, and the problems have been *prioritized* (**Table 2**), one can then use a systematic approach to attempt to modify the patient's lifestyle and medical therapy. In order to reduce the overall median blood glucose without causing an excessive risk of hypoglycemia, it is usually necessary to first reduce the variability of the blood glucose. After variability has been reduced, one can then increase the intensity of therapy to achieve a lower median blood glucose, with reduced risk of hypoglycemia (**Table 3**).

Table 3. A General Strategy to Reduce Variability in Blood Glucose

Step	Factors to Address
1. Identify and remove longitudinal component (by date)	Changes in treatment; intercurrent illness; effects of other medications; stress; travel; changes in lifestyle (diet, exercise), adherence; pharmacodynamics of medications (e.g., thiazolidinediones); long term titration of medications (e.g., long acting insulin analogs)
2. Identify and remove any variability in glucose control associated with day of the week	Lifestyle: schedule, exercise, diet, stress
3. Identify any systematic trend related to circadian (diurnal) patterns	Address possible over-treatment or under-treatment of nocturnal glycemia relative to daytime; diet; medications (e.g., metformin reducing nocturnal hepatic glucose output), insulin (balance of basal insulin and premeal bolus insulin)
4. Identify and remove variability related to post-prandial excursions	Diet (number of meals; calories, carbohydrate content and glycemic index of meals); timing of meals relative to insulin or other pre-meal medications (insulin secretagogues, alpha-glucosidase inhibitors); efficacy of medications; rate of gastric emptying as modified by the fat content of meals, gastroparesis, medications (e.g., exenatide, pramlintide)
5. Identify and reduce random variability at any specified time of day or associated with meals	Regularization of lifestyle: diet, exercise; education and motivation re adherence to medications, timing of medications, timing of meals, stress. Apply these considerations to all times of day
6. After the overall pattern has become stable, flat, and narrow, one can progressively intensify therapy to reduce the average level of glucose	Increase medications affecting glucose at all times of day gradually and with careful monitoring at all times of day

Table 3. An example of a systematic approach to *reduction of variability* in blood glucose. The total variability in blood glucose is composed of several components. It is important to be able to identify, measure, prioritize and introduce interventions to reduce each source of variability. After the total variability has been reduced, one can intensify therapy so as to reduce the median blood glucose and hence the A1c.

Discussion

Downloading of data from the glucose meter followed by display and analysis of SMBG data can help the physician in the management of patients with both Type 1 and Type 2 diabetes. This approach has been seriously underutilized. When patients observe that their glucose data are not being used effectively for their management, they may become less likely to monitor their blood glucose on a regular basis. There are several barriers to use of downloading that need to be addressed. Office workflow issues and reimbursement are important. The reports generated need to be improved to make them more informative, easily understandable, succinct, usable and user-friendly. It is important to have options for customization at many levels.

Statistical analyses should be simplified using methods that are easily comprehensible both by health care providers and by patients. The median, 25th and 75th percentiles, and Inter-Quartile Range (IQR) are important alternatives to use of the mean and standard deviation to characterize the central tendency and variability in the distribution of glucose. Graphical displays of glucose by date, time of day, relationship to meals, and day of the week should be accompanied by the median, 25th and 75th percentiles and IQR, with appropriate smoothing as needed to minimize random sampling variability. Extensive statistical analysis of the data should be performed in the background to assess dozens of potential patterns. The most significant patterns and clinically important problems can then be brought to the attention of the physician with statements presented in plain language text. Multiple types of graphs, statistics, and tables should be available as needed.

Variability of glucose had been underappreciated as a risk factor for complications[12-19] but remains controversial.[20] It is important to have a simple, readily understandable, reliable measure of variability. Further, we need norms for interpretation of variability in qualitative terms (excellent, fair, etc.). These criteria are strongly dependent on the median blood glucose value in order to control the risk of hypoglycemia.

We have presented a general, systematic strategy to assist the clinician in regard to: 1) analysis of glucose data and derived characteristics (**Table 1** and **Table 2**) identification and prioritization of potential clinical problems (**Table 2**, and **Table 3**), and reducing variability and translating the results of the SMBG analysis into adjustments of therapy so as to achieve improved glycemic control (**Table 3**). This approach is suggested as a prototype for further customization.

Several recent clinical studies (e.g., "GOAL A1c," "INITIATE," and "LANMET") have demonstrated improved levels of glycemic control using insulin analogs combined with algorithms for titration of insulin doses.[33-35] However, only a small percentage of patients achieved the target level for A1c of 6.5% as recommended by the American College of Endocrinology and International Diabetes Federation, and a modest number achieve the goal for A1c of 7.0% as recommended by the American Diabetes Association. We suggest that future clinical studies of this type should include measures of glucose variability at baseline and throughout the study. We speculate that including measures of glucose variability in the algorithms for adjustment of therapy (as in **Table 3** above) will help patients achieve further improvement in glycemic control.

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