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EDITORIAL

Improved Outcomes from Diabetes Monitoring: The Benefits of Better Adherence, Therapy Adjustments, Patient Education, and Telemedicine Support

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Diabetes is a disease of numbers. Patients are asked to monitor blood glucose (BG) levels, insulin doses, exercise, calories, blood pressure, and severity of symptoms on numerical scales. With so many numbers to keep track of, diabetes patients can benefit from monitoring devices to measure, store, and analyze data.[1] New sensors, software, communication technologies, and motivational methods are elevating real-time monitored data to a position of increasing importance as a key component of diabetes management.

Principles of Monitoring for Diabetes

Current and emerging technniques for monitoring diabetes are based on four principles; these are listed in **Table 1**. Diabetes monitoring diabetes leads to better outcomes, provided that patients demonstrate adequate adherence, use the monitoring to make therapy adjustments, receive adequate education on how to respond to the measurements, and utilize the emerging power of telemedicine support that is increasingly associated with medical monitors.

Monitoring of diabetes is currently being performed on at least six types of health measures; they are listed in **Table 2**. Furthermore, new sensors for physiological monitoring are currently being developed, and the list will surely expand in the next few years. This editorial focuses on monitoring of BG, continuous glucose, and closed-loop system performance.

Table 1.
Principles of Monitoring Patients with Diabetes

Monitoring can only improve outcomes if patients actually use the monitors as prescribed
The purpose of real-time monitoring is to adjust treatment in real time—not just to enter data into a log
Health care professionals must educate their patients about what to do with the monitored data
Smart monitors with telemedicine can now analyze data, recommend therapy, or send alerts

Table 2.
Health Monitoring Currently Being Performed by Patients with Diabetes on Themselves

1. BG
2. Continuous glucose
3. Closed-loop system performance
4. Adherence to oral medications
5. Blood pressure
6. Foot images
7. Exercise performed
8. Dietary intake

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Abbreviations: (HbA1c) glycated hemoglobin, (BG) blood glucose, (CGM) continuous glucose monitoring, (FDA) Food and Drug Administration, (GPS) global positioning system, (SMBG) self-monitoring of blood glucose

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Blood Glucose Monitoring

Self-monitoring of blood glucose (SMBG) has four main purposes. Purposes of this practice include (1) protecting by allowing immediate confirmation of low or high BG levels; (2) self-treating high or low BG levels by adjusting therapy to reach target glycated hemoglobin (HbA1c); (3) educating about the effects of diet, exercise, and other factors on BG levels; and (4) motivating healthy behavior. Methods for data management of SMBG data are listed in **Table 3**.

Table 3.
Methods for Data Management of Self-Monitored Blood Glucose Data

Logbook
Web-based software
Smart phone via cable
Wireless to central server and then to multiple communication systems, including smart phone, telephone, or fax

Data recorded by hand in logbooks are subject to reporting errors. In one study in France, subjects' BG values were recorded and stored by the BG monitors without their knowledge. Overreporting (by writing phantom values in a logbook) and underreporting (by omitting SMBG measurements from a written logbook) occurred for 19% and 12%, respectively, of the actual data points.[2] Patients frequently report during visits that they forgot to bring their logbooks or their monitors that contain a log of BG data. Many health care professionals assume that, in most of these cases, the patients did not actually test themselves as much as was requested, but this situation has not been formally studied. Only a technology that can automatically time stamp, store, and transmit SMBG data to a health care professional can eliminate the problem of forgotten logbooks and meters and deliver accurate monitoring data. Furthermore, for the stored and transmitted data to be useful, the system must analyze the data stream with pictorial graphical displays and calculated metrics.

Manufacturers of most BG monitors provide dedicated software for analyzing data from their monitor, which can be downloaded from the Internet onto a computer. Data is then uploaded into the software program either by cable or wirelessly. The analyzed data can then be printed and brought to the clinician's office.[3] An emerging method for analyzing BG data is to transmit the data from the glucose monitor to a server and back to the person's smart phone for data analysis and, in some cases, decision support. Data can be transmitted by cable from the monitor to the smart phone for automatic uploading or from the monitor directly into the smart phone (if there is a connection between the two devices) or by direct transmission from the monitor to a central server (without a cable or a smart phone). From the server, the information can be sent automatically to a computer or a smart phone. This process of automatic uploading is expected to become increasingly adopted even as many other numbers that are important in our lives are becoming stored on the Internet.[4]

Software Applications for Blood Glucose Data

Mobile software applications, known as apps, for analyzing BG data and other numerical measures of interest to patients with diabetes are becoming increasingly available. Mobile health care and medical app downloads globally are expected to reach 44 million users by the end of 2012 and 142 million users by 2016.[5] A survey of 21 patients with type 1 diabetes who had not previously worked with any diabetes apps determined that the seven most important features in a SMBG app, starting with the most important, were (1) ease of use; (2) communication with the meter; (3) wireless connectivity; (4) number of reports; (5) appearance of the screens; (6) price; and (7) ability to synchronize with an online account.[6]

A literature review of features of SMBG mobile diabetes applications ranked the most common features that accompanied display and analysis of SMBG data.[7] The six most common features are displayed according to rank and prevalence in **Table 4**.

Table 4.
Six Most Prevalent Features in Diabetes Apps in Addition to Self-Monitoring of Blood Glucose Data Analysis, According to Rank and Prevalence[7]

Rank	App feature	Prevalence
1	Insulin dosage	65%
2	Communication	59%
3	Diet	52%
4	Physical activity	40%
5	Weight	39%
6	Blood pressure	32%

Peripherals for Monitoring of Diabetes

The capabilities of smart phones are being extended by the attachment of peripheral equipment, or peripherals, that contain sensors.[8] Many of these sensors are wearable.[9] At this time, peripherals are not frequently used, but as the monitoring technology improves, it is expected that smart phones will be used as part of monitoring systems. An example of this process would be the use of a light and fluorometer to read the fluorescence lifetime of nano-optodes, which fluoresce according to the concentration of glucose in the ambient interstitial fluid.[10] The light and fluorometer could be a peripheral for a smart phone.[11] A touch screen has been developed to be a biomolecule detection platform.[12] This system is not currently intended for measuring glucose, but it is conceivable that a sheer disposable screen could be developed to fit over a smart phone and serve as a surface for measuring blood, urine, or saliva specimens to monitor analytes of interest in diabetes.[13,14]

Adherence to Monitoring

The use of SMBG in non-insulin-treated patients with type 2 diabetes is a controversial topic because some studies have demonstrated improved outcomes and some studies have failed to demonstrate improved outcomes.[15] The report of an expert panel that reviewed the literature and reported its findings in 2011 concluded that SMBG in this population should be performed in a structured format where the glucose data are used to guide treatment. New data from randomized controlled trials since 2008 have demonstrated the efficacy of this practice.[16] The need for using self-monitoring to guide treatment is a basic feature of all useful types of self-monitoring. Adherence to monitoring will be poor unless patients understand the reasons for monitoring and are taught what to do with the monitored information. The health care professional is obligated to teach the patient what to do with the information, or this tool will probably not be used properly and the monitoring will probably not achieve the intended outcome.

Continuous Glucose Monitoring

The American Association of Clinical Endocrinologists Consensus Panel on continuous glucose monitoring (CGM) reported their conclusions about the use of CGM. The key takeaway or summary of their conclusions for adults was, "More consistent CGM use predicts HbA1c reductions," and their key takeaway for youth was, "The best HbA1c-lowering results were seen in patients who used the sensor 6 to 7 days a week."[17] These conclusions were based on observations that, in intention-to-treat studies, subjects who use CGM more frequently have better outcomes than subjects who use CGM less frequently.

The STAR 1 trial evaluated the safety and efficacy of an insulin pump combined with use of a real-time CGM device compared with an insulin pump alone in subjects with type 1 diabetes already using insulin pump therapy. The HbA1c reduction was no different between the two groups. Subjects who used CGM during at least 60% of days had a significantly better HbA1c outcome than those who used CGM no more than 60% of days.[18] The landmark Juvenile Diabetes Research Foundation CGM study stratified type 1 subjects into three age groups: 25 years or greater, 15–24 years, or 8–14 years. The study demonstrated a benefit of CGM of 0.053%, a worsening of HbA1c of 0.08%, and a benefit of 0.013%, respectively. The use of CGM at least 6 days per week occurred in 83% of subjects ages 25 years or greater, 30% of subjects ages 15–24 years, and 50% of subjects ages 8–14 years. The authors concluded that the observed age effect on HbA1c might have been "related to substantially greater use of sensors in the adults than in patients in the two younger age groups."[19] Vigersky and colleagues[20] reported a randomized controlled trial of CGM in type 2 diabetes subjects. The study compared the effects of 12 weeks of intermittent real-time CGM with SMBG after a 40-week follow-up period. The subjects who used the CGM system per protocol (≥48 days) improved the most ($p < .0001$). These three studies of CGM demonstrated that, when CGM is actually used, the best outcomes occur.

Closed-Loop Systems

Closed-loop control studies have been performed mostly in inpatient studies to date. New trials will be getting underway in the United States and Europe to assess the performance of these systems in outpatients.[21] Modular architecture technology is being developed to monitor CGM results and insulin dosages of study subjects remotely.[22] Telemedicine systems are being developed to monitor various measures continuously and to contact study subjects immediately if necessary.[23] On July 22, 2008, at a Food and Drug Administration (FDA)/National Institutes of Health/Juvenile Diabetes Research Foundation workshop on artificial pancreas in Bethesda, I proposed a remote system to diagnose and fix problems of a closed-loop system. The system was named the Knowledge of Loop Operations Necessary System to Assist Repairs, whose acronym was Klonstar.[24] Dassau and associates[25] later proposed a specific telemedicine system based on Klonstar that was called an enhanced 911/global positioning system (GPS) wizard to prevent hypoglycemia, which integrated CGM with a hypoglycemia-predictive algorithm, with a GPS position locator and a short message service to monitor and alert for hypoglycemia. Furthermore, this system would be integrated with the patient's insulin pump to decrease or suspend insulin infusion in the event of impending hypoglycemia.[25] Currently, no closed-loop system is approved for use in the United States by the FDA. The first system with automatic control of insulin delivery, Veo, manufactured by Medtronic Diabetes, Northridge, CA, is available in Europe and Canada but has not yet been approved for use in the United States. This system contains hypoglycemic alarms for predicted and threshold levels of hypoglycemia but no remote telemedicine capabilities.[26] A remote warning system for use by CGM device users who might be experiencing unrecognized nocturnal hypoglycemia was approved by the FDA. The system consists of a monitor for the patient, a power supply, and a transmitter to send information to a second monitor at the bedside of another person in the house. The second monitor sounds a loud alarm in the event of hypoglycemia, which is intended to awaken the other person in case the patient develops nocturnal hypoglycemia and sleeps through the alarms.[27]

Conclusions

Many additional monitors for measuring, storing, and assessing information about new analytes and vital signs of interest for diabetes are expected to become available.[28–30] Patterns of glycemia over geographic space will be available with the use of GPS combined with CGM.[31] Reminders for overdue health maintenance services will be programmable into monitors used at home.[4] Increasing use of decision support software for real-time therapeutic maneuvers will add value to monitoring systems that accrue and analyze data.[32] Monitoring of BG and many other factors affecting the health of patients with diabetes will be successfully adopted for the benefit of patients (1) if the monitoring equipment is actually used by patients to make measurements; (2) if the information provided from these monitors is actually used by patients to determine therapy; (3) if the use of this equipment is supported by specific educational initiatives from health care providers; and (4) if monitoring systems can be integrated with online Web sites to store and analyze the monitored data. Monitoring for diabetes is in its infancy. This activity will increase in importance in parallel with anticipated advances in clinical chemistry, telemetry, and the pathophysiology of diabetes.

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