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CLINICAL APPLICATIONS

Actionable Self-Monitoring of Blood Glucose: Redefining the Role for Patients Using Multiple Daily Injection Therapy

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Abstract

Self-monitoring of blood glucose (SMBG) values is an accepted requirement for patients with diabetes using multiple daily injections of insulin. Nevertheless, for many patients, the full value of SMBG has yet to be realized due to a number of factors that contribute to patients not taking appropriate action based on the achieved result. The reasons for this are complex but are related to the burden imposed by performing the tests, the need for complex numerical calculations, and the demand for undertaking this activity multiple times each day.

In the near future, SMBG devices are likely to include technological innovations that are aimed at overcoming these barriers, offering "actionable" SMBG for patients using insulin. These innovations should include technologies that will allow customization and individualization based upon specific therapy regimens.

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Introduction

Blood glucose monitoring became a reality for the first time in 1964, when Ames Laboratories invented the dextrostick.[1] However, the concept of an easy and quick method of measuring blood glucose for patients with diabetes to monitor themselves was not considered until 1975.[2] Since then, self-monitoring of blood glucose (SMBG) has become an integral feature of modern diabetes care, although there is still controversy about its role in non-insulin-treated individuals.[3] For anyone considering the role of SMBG in diabetes management, an important caveat is that the benefit of testing must relate to appropriate actions being taken after obtaining the blood glucose value—"testing for the sake of testing" without considering the context of the result is of almost no value.[4]

On average, people with diabetes spend an hour each day on self-management of their condition.[5] Accordingly, the integration of SMBG into everyday diabetes care can add a significant social and psychological burden for patients,[6] and this may partially explain the observation that SMBG is performed infrequently by the majority of patients.[7]

Self-monitoring of blood glucose typically is also not a prominent topic in scientific discussions or conferences,

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Abbreviations: (MDI) multiple daily injection, (SMBG) self-monitoring of blood glucose

Keywords: blood glucose monitoring, bolus, calculation of insulin dose, diabetes management, insulin, meal, self monitoring

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but it is by-in-large accepted as an integral part of modern insulin therapy. There exists an opportunity to explore the current role of SMBG and examine the potential for novel approaches to blood glucose monitoring. This is particularly relevant as new technologies and therapeutic options become available for diabetes care. Possible development opportunities include personalized and "actionable" feedback loops based on recent test results as well as specific recommendations for therapy adjustment such as insulin dosing suggestions. In essence, *actionable* SMBG offers the potential to assist patients beyond just providing a blood glucose reading at a single moment in time.

The Value of Self-Monitoring of Blood Glucose

An accurate blood glucose reading can support a patient's self-management and aid physicians' therapy recommendations in a number of areas (**Figure 1**). For insulin-treated patients, SMBG is used first and foremost (a) as an early warning to detect or confirm hypoglycemia; (b) to assess the prevailing level of blood glucose control; (c) to provide guidance on making changes to therapy, e.g., altering the dose, timing, or frequency of basal insulin,[8] or making changes in therapy regimen; and (d) to provide data on which immediate therapeutic decisions are made, e.g., adjusting the dose of rapid-acting insulin to cover a meal.[9] Moreover, SMBG has the potential to help patients better understand the impact of lifestyle modifications (exercise/diet) or life events (sickness/travel) on glycemic control.

From **Figure 1**, it is clear that the potential value of SMBG increases with the complexity of the therapeutic regimen. For example, with patients using multiple daily injections (MDIs), the SMBG value is critical to the calculation of a safe and appropriate mealtime insulin bolus dose based on actual glycemic status.

Insulin Dose Adjustment

Conceptually, for patients using MDI therapy, the derivation of an appropriate insulin dose for a given meal can be structured into three "activity" phases (**Figure 2**).

The first phase "blood glucose measurement" is supported by modern blood glucose measurement systems, most of which are easy to use and provide a patient their current blood glucose value. Phase two represents the calculation of an appropriate insulin dose, which—depending on the regimen—can be quite complex and, for the majority of patients, is at present not supported by technology. Phase three represents the administration of insulin with a syringe or pen device.

The Scientific and Pragmatic Foundation for Self-Monitoring of Blood Glucose

For patients with type 1 diabetes, the introduction of the concept of "intensive" insulin therapy in the Diabetes Control and Complications Trial established the role of SMBG as part of a multicomponent diabetes regimen for this population.[10] However, several systematic reviews have highlighted the controversies of SMBG, particularly in patients with non-insulin-treated type 2 diabetes, but this partially may be a reflection of the shortcomings of the studies rather than the technology behind SMBG.[11]

It is difficult to design appropriate randomized controlled clinical trials to determine the effect of SMBG in isolation from other interventions. There are also few, if any, clinical trials comparing different frequencies and timings

	THERAPY REGIMEN	Lifestyle (Diet & Exercise)	Oral anti-hyperglycemic agents	Oral hypoglycemic agents (sulfonylureas)	Incretins	Basal insulin	Pre-mixed insulin	Intensive insulin therapy (MDI)	Who takes action?
VALUE OF SMBG	Detection of hyperglycemia (impact of food & lifestyle)	√							*Informing patient action*
	Optimization of medication, dosing & timing		√	√	√	√	√	√	*Informing HCP actions*
	Changes in therapy	√	√	√	√	√	√	√	*Informing HCP actions*
	Detection of hypoglycemia			√		√	√	√	*Informing patient action*
	Insulin dose titration					√	√	√	*Informing patient action*
	Insulin dose adjustment (actual glycemic status)							√	*Informing patient action*

Figure 1. Current potential value from structured SMBG by therapy regimen. HCP, health care practitioner.

of SMBG testing regimens. Despite almost universal agreement that SMBG should be available to all individuals with diabetes treated with insulin, the actual evidence to support this recommendation is somewhat minimal.[12]

Future clinical trials of SMBG should evaluate the value of technological innovations in the context of changing treatment algorithms, new models of care, and evolving standards of testing (frequency and timing). In order to fully understand the complex and intensive interaction of a patient with their monitoring and therapy recommendation device, it is important to capture and analyze patient-specific motivational aspects and individual skill sets when interpreting study results. Quite possibly, various patient populations will obtain differing degrees of benefit interacting with the new devices, which may be in part due to inherent patient factors. Understanding these aspects should allow for development of educational materials and supporting health care provider tools to improve initiation of new patients to these devices and support the continued use in different stages of their diabetes "journey." Furthermore, comparisons will need to be made of actionable SMBG to continuous glucose monitoring systems with the latter supplemented by algorithms for treatment change.

Reviewing current SMBG literature, we observe the following.

- Most studies have not examined the role of SMBG as an intervention on its own.
- In some studies, no action was taken based on the results. In only a small number of studies were patients encouraged to adjust their treatment based on SMBG values. As a corollary, some studies implied that SMBG should be carried out to inform the health care professional rather than the patient.
- Many studies do not provide information on outcomes according to the treatment used (i.e., combinations of oral therapy with insulin and various insulin regimens). Consequently, it is difficult to determine if one particular treatment regimen gains added value from SMBG compared with another.
- Additional studies have not linked SMBG with appropriate training, feedback, or treatment modification with the potential for behavior change.
- There is limited guidance from trials as to whether specific patient factors are important in determining the impact of SMBG, e.g., age, gender, educational level, or socioeconomic status.
- The impact of patient concerns such as inconvenience and pain may influence the frequency of testing and value of the data. This aspect is invariably not considered in large clinical trials.

It is also surprising that, in trials of insulin initiation in type 2 diabetes, algorithms for insulin dose titration based on SMBG values are not always included in the protocol and details about the training of participants to be able

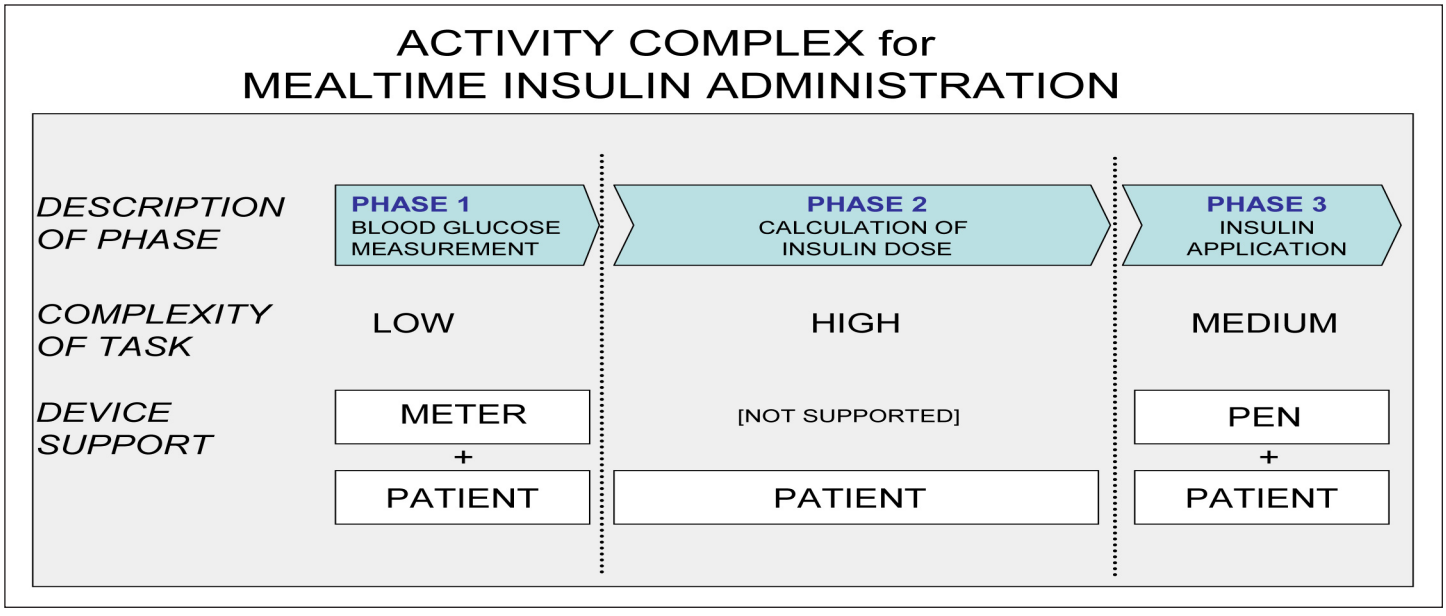

Figure 2. The insulin activity complex comprises three phases: blood glucose measurement, calculation of insulin dosage based on several patient-specific factors, including the SMBG result, and insulin dose administration.

to make their own treatment adjustments are frequently not described.[13,14]

Inadequate Insulin Administration

For insulin-treated individuals at risk of hypoglycemia, accuracy of the SMBG technology is an important consideration.[15] The accuracy of SMBG can be affected by technical factors such as extremes of hematocrit or oxygen saturation or the presence of interfering substances.[16,17] There are also patient-related factors than can cause accuracy problems for any SMBG system, including the failure to wash hands before testing or using strips that are out of date.[9]

However, the process of moving from obtaining an SMBG result to administering an appropriate and accurate dose of insulin has a number of potential points for significant error. These include variations in insulin absorption based on the injection site, the impact of recent exercise, differences in glucose absorption due to different meal constituents and alterations in gastric emptying. Insulin dose adjustment and administration can be further complicated by physical limitations such as visual impairment or manual dexterity.[18]

For people living with diabetes treated with insulin, adherence to blood glucose testing and medication also appears to be influenced by regimen complexity. This includes the number of insulin injections, individual perception of side effects, the intrusion of medication on personal aspects of daily living cost, and concerns about excessive weight gain.[19,20] In everyday life, the frequency of SMBG testing may also be influenced by the anticipated outcome (i.e., why do a test if the result is expected to be much higher than ideal?) and the personal disruption caused by performing the test.[21]

Recently, there is growing awareness that defining and adjusting the frequency and timing of SMBG testing has the potential for facilitating positive behavior change. In non-insulin-treated patients, more structured SMBG combined with physician and patient training in interpreting preclinic visit 7-day SMBG profiles is associated with modest improvements in glycemic control without requiring an increase in the overall frequency of testing.[22] This type of structured approach needs to be assessed in insulin-treated individuals. Where mealtime rapid-acting insulin is added to basal insulin, meaningful improvements in blood glucose control can also be achieved using simple algorithms for altering the insulin dose based on pre-meal SMBG values.[23]

Mealtime Insulin Dosing: A Complex Task

For patients using MDI therapy combined with carbohydrate counting, this regimen requires skill at handling numbers in order to calculate accurate and safe insulin doses. As mentioned earlier, when calculating a mealtime dose of insulin, patients need to integrate multiple inputs, including the carbohydrate content of food, insulin-to-carbohydrate ratio, current glucose level, target glucose level, as well as the correction factor. They also need to consider the residual effect of the previous insulin injection.

Adherence to diabetes treatment and monitoring regimens are difficult for all patients but particularly so for the underprivileged or those with low socioeconomic status, people with depression, the low literate, and those with English as a second language.[6,24–26] Therefore, difficulty in handling numbers is very likely to impact negatively on a patient's attempts to achieve optimum control of blood glucose levels.

Self-Monitoring of Blood Glucose in the Future: The Role of Technology

Changes in consumer electronics have altered markedly methods of communication and facilitated engagement between vast numbers of people. For example, email and text messaging used in supporting diabetes management have been shown to be viable and acceptable; however, maintaining participants' interest remains a challenge.[27] There is evidence that smartphones can be used for delivering patient education. Teaching patients about carbohydrate counting via a mobile phone has been shown to reduce hemoglobin A1c levels similar to that achieved by "traditional" structured patient education programs but requires significantly less health care provider resource.[28] In a meta-analysis assessing the impact of mobile phone interventions on glycemic control, Liang and colleagues[29] assessed 22 studies involving more than 1600 participants and reported that this type of intervention led to a reduction in hemoglobin A1c of the order of 0.5% and that mobile phone interventions are especially valuable for patients with type 2 diabetes.

To overcome previously listed challenges in achieving optimum diabetes control, manufacturers of new devices need to consider the patients' barriers to successful intensive insulin therapy during product development.[30] This implies thinking about factors directly related to user–device interactions, e.g., patient competency and behavioral aspects (motivational aspects) as well as health

care system constraints. Device manufacturers could include tools to accomplish the following:

- Enable patients to act on their blood glucose results
    - Translate blood glucose test results into actionable information and advice for diabetes management
    - Bolus and basal insulin calculators for patients using MDI therapy
- Support transfer and management of blood glucose data
    - At a simple level, this would be a data capture system to facilitate a discussion between patients and their health care providers.
    - Devices for supporting home monitoring and care at a distance from specialist centers (tele-monitoring and telehealth)
- Assist with interpretation of data
    - Aids for interpretation of SMBG data in the form of pattern recognition of hypoglycemia and/or hyperglycemia recurrence.
    - Subsequent developments could include specific prompts for clinicians about potential reasons for these events occurring (e.g., inadequate insulin dosing, wrong time of administration of a bolus dose, or insulin stacking due to too frequent bolus dosing), and further advancements could include decision support technology or predictive modeling based on potential changes in therapies
- Support behavioral changes: adherence to testing and therapy
    - Create a structured approach to SMBG for specific needs, e.g., the use of regular testing and carbohydrate-free meals to assess the efficacy of a prescribed basal insulin dose and encourage greater use of paired preprandial and postprandial testing to optimize the timing and dose of mealtime insulin
    - Telephone, Web, and mobile phone applications to aid learning and applying new technologies that take into account an individual's achieved level of numeracy and literacy in addition to native language, culture, and age
    - Systems for supporting behavior modification for overweight or obese subjects
    - Using new social media to deliver education and peer support and for providing immediate user feedback on a device.

Advances in technology need to be easy to use and manageable as well as meet specific unmet needs of patients in order to be meaningful. This requires not only gaining insights into the specific challenges of insulin management within a patient population but also a rigorous and continuous research effort to understand device value in different settings of health care. Additionally, this research should be used to further improve a "device feature" as well its user interface. Increased intensive design research efforts and human factors testing are preceding clinical testing to then prove the benefit of a new blood glucose device. Ideally, such a device of the future will be customizable to different settings of care without requiring complicated setup methods and a steep user learning curve.

We speculate that such devices in the future will be further inspired by approaches that have been successful in engaging with consumers in the computer gaming industry. An additional approach would be to create technologies based around common "life events" for individuals living with diabetes such as technologies to support travel, shift work, or in-hospital care, where it may be possible to predefine frequency and timing of SMBG to maximize benefit and reduce risk. It is also anticipated that future technologies will be personalized to current treatment regimens. For example, the optimum approach to SMBG may be varied according to treatment regimen and target population, including hypoglycemia risk as well as an individual's short- and long-term glycemic goals. Along with being drivers of empowerment for an individual, these types of technological advances may increase the opportunities for other health care professionals, e.g., pharmacists to be more closely involved in diabetes care.

New technology should provide opportunities for SMBG to become more relevant for individual patients, by delivering actionable advice to support diabetes management. As a first step, in addition to measuring blood glucose, actionable SMBG devices should incorporate the following:

1. Customization and individualization per specific therapy regimens, i.e., the device is a support tool for an individual's therapy, and

2. Consideration for personal aspects of daily living that impact an individual's ability to achieve their desired glycemic control.

In the past, most devices only measured a single blood glucose value in isolation. By adopting new, actionable SMBG technologies, we believe patients will be enabled to self-manage their condition better and, in the longer term, potentially reduce the burden of diabetes on the individual and society.

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