

## COMMENTARY

# Self-monitoring of Blood Glucose in Individuals with Type 2 Diabetes Not Using Insulin: Commentary

Self-monitoring of blood glucose (SMBG) is a diagnostic test that has enhanced diabetes self-management, especially for individuals with type 1 diabetes and those with type 2 diabetes using insulin. SMBG provides instant information about blood glucose (BG) and allows detection of hypoglycemia or hyperglycemia, which can enable individuals with diabetes to achieve glycemic targets by making safe and appropriate treatment and/or lifestyle/nutritional changes.

There is conflicting evidence regarding the benefit of SMBG in individuals with type 2 diabetes taking oral antihyperglycemic agents. Indeed, SMBG confers a considerable cost to both the individual with diabetes and healthcare providers, and can be uncomfortable to perform for many individuals. Several large clinical trials (the United Kingdom Prospective Diabetes Study [UKPDS], the Action to Control Cardiovascular Risk in Diabetes [ACCORD] and the Action in Diabetes and Vascular Disease [ADVANCE], utilized structured recommendations of SMBG to achieve intensive glycemic control (1-3). These studies did not specifically assess the utility of SMBG; rather, they assessed the risks and benefits of intensive vs. conventional glycemic control. SMBG was used in these studies for the prevention of hypoglycemia and modification of nutritional therapy, physical activity and pharmacologic therapies. Therefore, SMBG is a useful tool for patient safety and guidance of therapy, but is not a therapy in and of itself.

## SMBG and Hypoglycemia

Clinical trials are not designed to achieve an outcome of hypoglycemia, primarily due to patient safety and ethical concerns. As a result, clinical studies of SMBG are lacking with respect to the relationship between hypoglycemia and SMBG. Therefore, determining if SMBG is useful for the prevention of hypoglycemia must be done indirectly.

Hypoglycemia is associated with many known adverse effects. The psychological impact of hypoglycemia is also an important factor to consider, as fear of hypoglycemia contributes to anxiety and lack of treatment adherence (4-6), placing individuals at risk for complications of diabetes in order to prevent hypoglycemia. Hypoglycemia has also been associated with higher rates of dementia (7).

To better define the appropriate frequency of SMBG,

factors that contribute to the risk of hypoglycemia among patients with type 2 diabetes on oral antihyperglycemic agents must be considered. Insulin secretagogues and insulin are associated with more severe hypoglycemia; it is estimated that up to 10% of sulfonylurea-associated hypoglycemia may be fatal (8,9). Among the insulin secretagogues, glyburide has one of the highest risks of hypoglycemia (10), especially in the elderly, who are already at higher risk for hypoglycemia (11); therefore, more frequent SMBG may be required in this population.

Conversely, many oral antihyperglycemic agents have a low risk for severe hypoglycemia when used as monotherapy or in combination. Therefore, SMBG would not be required for detection of hypoglycemia in most individuals taking these medications.

The risk of hypoglycemia increases with duration of diabetes in individuals with type 1 or type 2 diabetes. Therefore, the frequency of SMBG may need to be increased the longer the duration of diabetes (12). Hypoglycemia unawareness also occurs in type 2 diabetes and is an important consideration for SMBG (13).

Hypoglycemia represents a huge healthcare burden. In the United States, from 1993 to 2005, >5 million emergency room visits occurred due to hypoglycemia, 25% of which resulted in a hospital admission and 44% of which occurred in adults aged  $\geq 65$  years of age (14).

## SMBG and Glycemic Control

### *Observational studies*

Observational studies for SMBG show conflicting evidence of the role of SMBG in glycemic control. These studies are more numerous than randomized controlled trials (RCTs) and show that SMBG is associated with both improved glycemic control (15-17) and no improved glycemic control (18-20). Observational studies present multiple challenges regarding interpretation and are highly heterogeneous; for example, individuals with poorer glycemic control are more likely to be asked to perform SMBG, thereby confounding the results (19). Other factors not captured in observational studies include concomitant medical conditions and medications, occupation, intercurrent illnesses, education levels, socioeconomic status, ethnic background, gender, exercise regimens and meal patterns. Many of these factors influence both the amount of SMBG performed as well as the inter-

pretation of study results (21).

Currently, no trial has been conducted with a structured self-management education component as part of the SMBG intervention against SMBG alone. This is a major criticism preventing meaningful interpretation of the ability of SMBG alone to influence glycemetic control. As well, several of the published trials enrolled patients with reasonable glucose control (i.e. mean A1C  $\leq$ 7.5%); thus, the expected benefit of SMBG is limited. Trials involving those with higher baseline mean A1C have demonstrated greater reduction in A1C, as would be expected.

Outcome studies of SMBG have also shown conflicting results. The Fremantle Diabetes Study demonstrated decreased cardiovascular events in some subgroups but higher cardiovascular events in others, and decreased retinopathy (22). The Retrospective study Self-monitoring of Blood Glucose and Outcome in Patients with Type 2 Diabetes (ROSSO) study showed that SMBG was associated with decreased diabetes-related severe morbidity and all-cause mortality (23).

### Randomized controlled trials

The Diabetes Glycaemic Education and Monitoring (DiGEM) study found that SMBG had no significant benefit in patients with type 2 diabetes (24). This study randomized 453 patients with type 2 diabetes with a mean A1C of 7.5% to 3 groups (standard care; standard care plus SMBG; and standard care plus SMBG and patient training regarding interpretation of results). The intensive group had a non-significant 0.17% lowering of A1C, which prompted the authors to conclude that SMBG with or without education was not useful in this population. However there were multiple limitations: the study population was small and the relatively low A1C level of 7.5% means it would be difficult to show that a diagnostic test could improve this level significantly. Compliance with intensive monitoring was poor (52%) and 12% of patients were lost to follow-up. Moreover, lower A1C may not motivate patients to further improve their glycemetic control. Other limitations include no information gathered by the authors regarding pre- and postprandial BG levels.

A 6-month RCT was conducted in 21 centres in Germany and Austria in non-insulin-using individuals with type 2 diabetes (25). SMBG was used as a tool for patient empowerment regarding self-management, which was structured around meals. Both the control and intervention groups showed lowered mean A1C levels, which were significantly improved in the SMBG group ( $-1.0\%$  vs.  $-0.54\%$ ). There were also improvements in well-being and lower depression scores. Similarly, the Auto-Surveillance Intervention Active (ASIA) study of non-insulin-using individuals with type 2 diabetes demonstrated that SMBG was associated with lowered A1C (26).

### Systematic reviews

A meta-analysis by Welschen and colleagues assessed the effects of SMBG relative to usual care without SMBG on BG control, quality of life and well-being, patient satisfaction and hypoglycemic episodes, in people with type 2 diabetes not on insulin (27). Six RCTs conducted between 1996 and 2004 were identified. There was a slight statistically significant decrease in A1C of 0.39% in favour of SMBG, compared with the control group.

McAndrew and colleagues conducted a systematic review of relevant studies on the impact of SMBG on A1C levels in people with type 2 diabetes from 1990 to 2006, all of which included people with type 2 diabetes not using insulin (28). Twenty-nine studies met the inclusion criteria (9 cross-sectional studies, 9 longitudinal studies and 11 RCTs). Evidence from the cross-sectional and longitudinal studies was inconclusive, while evidence from the RCTs suggested that SMBG may lead to improved glycemetic control (28).

A recent meta-analysis by Poolsup and colleagues assessed the benefits of SMBG in individuals with type 2 diabetes (29). Only RCTs where the assessment was A1C level were included. SMBG was found to be effective in reducing A1C levels in non-insulin-treated type 2 diabetes (pooled mean difference,  $-0.24\%$ ; 95% CI,  $-0.34\%$  to  $-0.14\%$ ;  $p < 0.00001$ ). In particular, SMBG proved useful in the subgroup of patients whose baseline A1C was  $\geq 8.0\%$  (29).

### SMBG AND GUIDELINES

A number of clinical practice guideline committees around the world have made recommendations regarding SMBG (30-34). A summary of these recommendations is provided in Table 1. In general, these guidelines acknowledge the benefit of SMBG in individuals with type 2 diabetes not using insulin. However, the guideline committees all noted that further study is needed and that the current literature provides no clear guidance due to differences in study designs, populations and interventions.

### CONCLUSIONS

There are 2 major considerations regarding the appropriateness of SMBG in individuals with type 2 diabetes. The first is patient safety, particularly with respect to hypoglycemia. Assessment of the risk factors for hypoglycemia include type of medication, age, job status, activity, meal patterns, illness and concomitant medical conditions. The second consideration is that SMBG can be used to motivate and enable individuals and their caregivers to receive instant feedback regarding their BG levels so that their diabetes management is optimized and diabetes complications are prevented. SMBG is a valuable resource and as such should be used appropriately; inappropriate use will lead to wastage and higher costs for the individual, as well as private and public payers.

<b>Table 1. SMBG guideline recommendations</b>	
<b>Organization</b>	<b>Recommendations</b>
American Diabetes Association (31)	<ol style="list-style-type: none"> <li>1. SMBG should be carried out three or more times daily for patients using multiple insulin injections or insulin pump therapy.</li> <li>2. For patients using less frequent insulin injections, noninsulin therapies or medical nutrition therapy alone, SMBG may be useful as a guide to the success of therapy.</li> <li>3. To achieve postprandial glucose targets, postprandial SMBG may be appropriate.</li> <li>4. When prescribing SMBG, ensure that patients receive initial instruction in, and routine follow-up evaluation of, SMBG technique and their ability to use data to adjust therapy.</li> </ol>
Canadian Diabetes Association (30)	<ol style="list-style-type: none"> <li>1. For individuals treated with oral antihyperglycemic agents or lifestyle alone, the frequency of SMBG should be individualized depending on glycemic control and type of therapy and should include both pre- and postprandial measurements.</li> <li>2. In many situations, for all individuals with diabetes, more frequent testing should be undertaken to provide information needed to make behavioural or treatment adjustments required to achieve desired glycemic targets and avoid risk of hypoglycemia.</li> <li>3. In order to ensure accuracy of BG meter readings, meter results should be compared with laboratory measurement of simultaneous venous FPG at least annually and when indicators of glycemic control do not match meter readings.</li> </ol>
Diabetes Australia (32)	<ol style="list-style-type: none"> <li>1. SMBG should be considered in all people with type 2 diabetes but the decision to perform SMBG, and the frequency and timing of testing, should be individualized.</li> </ol>
International Diabetes Federation (33)	<ol style="list-style-type: none"> <li>1. SMBG should be considered at the time of diagnosis to enhance the understanding of diabetes as part of their education and to facilitate timely treatment initiation and titration optimization.</li> <li>2. SMBG should also be considered as part of ongoing diabetes self-management education to assist people with diabetes to better understand their disease and provide a means to actively and effectively participate in its control and treatment modifying behavioural and pharmacologic interventions as needed.</li> <li>3. SMBG should be used when individuals with diabetes and/or their healthcare providers have the knowledge, skills and willingness to incorporate SMBG and therapy adjustment into their care plan in order to attain agreed treatment goals.</li> <li>4. SMBG protocols (intensity and frequency) should be individualized to address each individual's specific educational/behavioural/clinical requirements (identify/prevent/manage acute hyper- and hypoglycemia) and provider requirements for data on glycemic patterns and monitor impact of therapeutic decision making.</li> <li>5. The purpose(s) for performing SMBG should be agreed between the person with diabetes and the healthcare provider. These agreed upon purposes/goals and actual review of SMBG data should be documented.</li> <li>6. An easy procedure for patients to regularly check on their glucose meter performance should be a requirement for SMBG use.</li> </ol>
National Institute for Health and Clinical Excellence, United Kingdom (34)	<ol style="list-style-type: none"> <li>1. Offer SMBG to a person newly diagnosed with type 2 diabetes only as an integral part of his or her self-management education. Discuss its purpose and agree how it should be interpreted and acted upon.</li> <li>2. SMBG should be available: <ul style="list-style-type: none"> <li>• to those on insulin treatment</li> <li>• to those on oral glucose lowering medications to provide information on hypoglycemia</li> <li>• to assess changes in glucose control resulting from medications and lifestyle changes</li> <li>• to monitor changes during intercurrent illness</li> <li>• to ensure safety during activities, including driving.</li> </ul> </li> <li>3. Assess at least annually and in a structured way: <ul style="list-style-type: none"> <li>• self-monitoring skills</li> <li>• quality and appropriate frequency of testing</li> <li>• use made of the results obtained</li> <li>• impact on quality of life</li> <li>• continued benefit</li> <li>• equipment used.</li> </ul> </li> </ol>

BG = blood glucose

FPG = fasting plasma glucose

SMBG = self-monitoring of blood glucose

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