Guideline

Self-Monitoring

of Blood Glucose in Non-Insulin Treated Type 2 Diabetes

unite for diabetes

International Diabetes Federation

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Self-Monitoring of Blood Glucose in Non-Insulin-Treated Type 2 Diabetes
Recommendations based on a Workshop of the International Diabetes Federation Clinical Guidelines Taskforce in collaboration with the SMBG International Working Group

Website
This document will be available at www.idf.org and at www.smbg-iwg.com.

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1. Introduction

In October, 2008, the International Diabetes Federation (IDF) Clinical Guidelines Taskforce, in conjunction with the SMBG International Working Group, convened a workshop in Amsterdam to address the issue of SMBG utilization in people with type 2 diabetes (T2DM) that is not treated with insulin. Workshop participants included clinical investigators actively engaged in self-monitoring of blood glucose (SMBG) research and research translation activities. The purpose of the workshop was to:

- Review the findings of selected key studies that describe the clinical and metabolic impact and the cost implications of SMBG.
- Identify additional studies and study designs that are needed to further define the role of SMBG in non-insulin-treated people with T2DM.
- Propose recommendations for the use of SMBG in non-insulin-treated people with T2DM.

The following report presents a summary of the findings and recommendations related to the use of SMBG in people with non-insulin-treated type 2 diabetes.

2. Summary of recommendations

Findings from studies of SMBG used in non-insulin-treated T2DM have been inconsistent due to differences in study designs, populations, and interventions used. However, the data available from randomized controlled trials (RCTs) suggest that SMBG is likely to be an effective self-management tool only when results are reviewed and acted upon by healthcare providers and/or people with diabetes to actively modify behaviour and/or adjust treatment.

Although further studies are needed to better assess the benefits, optimal use and cost-effectiveness of SMBG, the following recommendations are proposed to guide individuals with non-insulin-treated diabetes and their healthcare providers in the use of SMBG.

1. SMBG should be used only when individuals with diabetes (and/or their care-givers) and/or their healthcare providers have the knowledge, skills and willingness to incorporate SMBG monitoring and therapy adjustment into their diabetes care plan in order to attain agreed treatment goals.
2. SMBG should be considered at the time of diagnosis to enhance the understanding of diabetes as part of individuals' education and to facilitate timely treatment initiation and titration optimization.

3. 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 pharmacological interventions as needed, in consultation with their healthcare provider.
4. SMBG protocols (intensity and frequency) should be individualized to address each individual's specific educational/behavioural/clinical requirements (to identify/prevent/manage acute hyper- and hypoglycaemia) and provider requirements for data on glycaemic patterns and to monitor impact of therapeutic decision making.
5. The purpose(s) of performing SMBG and using SMBG data 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.
6. SMBG use requires an easy procedure for patients to regularly monitor the performance and accuracy of their glucose meter.

A detailed explanation of these recommendations is presented later in the document (Recommendations, page 16).

The IDF uses three classifications of levels of care to promote cost-effective, evidence-based care in different settings where resources vary. The recommendations presented in this document are proposed as Standard Care, although it is recognized that the implementation of these recommendations in many parts of the world may be limited due to the lack of resources. Addressing resource deficiencies related to SMBG use is beyond the scope of this review. We therefore strongly urge the global healthcare community (providers, payers and industry) to develop innovative and cost-effective processes and products that will make SMBG accessible to people with diabetes who reside in these areas.

3. Background

Diabetes mellitus is a significant and growing global health problem, recognized by the World Health Organization and the IDF. In 2007, it was estimated that there were 246 million adults with diabetes throughout the world, with an increase in this number to 380 million expected by 2025 [1].

In 2006, the General Assembly of the United Nations unanimously adopted a resolution (61/225) which recognizes that diabetes is a global pandemic posing a serious threat to global health, acknowledging it to be a chronic, debilitating, and costly disease associated with major complications [2]. Diabetes reduces the quality of life, can generate multi-system morbidities and premature death, and consequently increases healthcare costs. Currently, in many countries, people with diabetes have a significantly decreased life expectancy [1].

Large, long-term, randomized controlled trials in both type 1 diabetes (T1DM) and T2DM have shown that aggressive treatment of hyperglycaemia significantly reduces the development and progression of microvascular complications [3-7]. A weaker relationship is observed in most studies between hyperglycaemia and the development/progression of macrovascular disease [8-12]. However, recent RCTs have not shown a benefit of tight glucose control on macrovascular disease in people with T2DM of long duration and high cardiovascular risk [7;13;14]. In the earlier studies, the benefits of tight control on macrovascular outcomes were seen only many years after the initial trial had ended and when levels of glycaemic control in the intervention and control arms had converged [11;15]. This so called 'metabolic memory' or 'legacy effect' suggests that, while the short-term benefits of tight glycaemic control for macrovascular disease have not been shown in RCTs [3;6], the longer-term benefits may be substantive [11;15] particularly when good HbA_{1c} levels are achieved and maintained early in the course of the disease. The longer-term findings suggest that greater benefits (clinical and economic) are obtained when simultaneous control of glycaemia, blood pressure and lipid levels has been achieved [16;17].

Although the use of SMBG is recommended in T1DM and insulin-treated T2DM individuals, there is no analogous consensus on the utility of SMBG in people with non-insulin-treated T2DM [18-22], mainly because of inconsistent results from randomized controlled trials as well as from observational studies.

Given the significant and increasing prevalence of diabetes worldwide and the economic costs associated with SMBG use, primarily due to an increase in T2DM in developing countries, there is a clear need to evaluate the clinical, metabolic and cost-effectiveness of SMBG.

4. Review of selected evidence

It was not the intention of the workshop to conduct a comprehensive review of the literature. Several recent reviews and meta-analyses provide such information [23-27]. The goal of this review was to evaluate the more recent and large published studies to identify the key relevant issues relating to the use of SMBG, the limitations of the selected studies, and to examine the seemingly controversial findings.

Observational studies

Among the observational studies considered were two of the largest follow-up studies of the association of SMBG with metabolic control (HbA_{1c}), Kaiser Permanente [28] and QuED [29], and the only two observational studies of the association of SMBG with clinical outcomes, ROSSO [30] and Fremantle [31].

Although observational studies cannot determine causality, they provide valuable insight into SMBG-associated outcomes under conditions of routine patient care. Three of the four studies (Table 1A) indicate that SMBG is preferentially introduced in patients with poor metabolic control. Two of these studies provided data before and after initiation of SMBG and observed improvement of HbA_{1c} values [28;32]. Similar improvement was also observed in non-pharmacologically treated patients, suggesting that SMBG has a positive impact on patients' lifestyle. Two studies covered a period of 5 or more to 6.5 years, which also allowed an assessment of the impact of SMBG on diabetic complications [28;30;30;31].

The ROSSO study reported a decreased risk/hazard ratio for non-fatal endpoints (mostly macrovascular) in non-insulin-treated T2DM patients (0.72 after multiple adjustments) [30]. The Fremantle Diabetes Study found a trend also for less macroangiopathy in such patients (hazard ratio 0.74, not significant), but cardiac mortality was higher in SMBG users (hazard ratio 0.93 before, 1.79 after multiple adjustments) [31]. The Fremantle Diabetes Study and ROSSO study differed in that the former required consent and active participation by recruited participants. In addition, the Fremantle Diabetes Study recruited people with diabetes irrespective of diabetes duration, while the ROSSO study started at the time of diagnosis. As a consequence most patients in the Fremantle study were already using SMBG at baseline (69%, increasing to approximately 85% within 3 years), whereas no patient performed SMBG at baseline in the German study [30], and SMBG usage (for at least one year) remained slightly below 50% during the follow-up period of 6.5 years. Hence, the Fremantle Diabetes Study resembles a cross-sectional design with only a minority not performing SMBG, whereas the ROSSO study starts from diabetes diagnosis with comparable group sizes of SMBG users and non-users during follow-up.

Randomized controlled trials

The registry of the SMBG International Working Group lists 22 RCTs of SMBG in non-insulin-treated T2DM (www.smbg-iwg.com). Some of these trials did not clearly group subjects by type of diabetes and treatment, were of small size and/or of short duration (3 months) or did not include a control arm without SMBG. Since the year 2000 six trials have overcome these shortcomings and five of them were analyzed in detail at the Workshop [18-20;22;33]. The sixth trial (ASIA study) reported a significantly lower HbA_{1c} level in the treatment arm using SMBG [21]. The comments below also apply to this study.

Table 1B shows a summary of the RCTs presented at the Workshop. A basic difficulty in drawing summarizing conclusions is that the clinical trials of SMBG compare interventions whereas SMBG is a diagnostic measure used for guidance by patients, healthcare providers or both, but is not a therapeutic intervention. Unfortunately, the SMBG-associated clinical intervention differs widely between the various RCTs [34]. Nevertheless, examination of these selected and other, more recent, trials allows several tentative conclusions.

The King-Drew Medical Center Trial [20] reported improvement of mean HbA_{1c} in both control and intervention groups, independent of SMBG. In this study, however, there was a rapid upgrading of medication by a nurse every two weeks if fasting plasma glucose was ≥ 130 mg/dl (7.2 mmol/l) without knowing either SMBG status or SMBG data. Thus, probably the frequent intensifying of medication in both groups overrode any potential to demonstrate benefit associated with SMBG.

The ESMON [33] and the DINAMIC I [19] trials appear to be further examples where intensive advancement of medication soon after diabetes diagnosis limited the possible added benefit of SMBG. In the ESMON trial, subjects were recruited soon after diagnosis of T2DM and intensive education and treatment resulted in a decrease of mean HbA_{1c} levels after 12 months from 8.6 to 6.9% in the control group, and from 8.8 to 6.9% in the SMBG group [33]. The DINAMIC I trial recruited subjects with early or mild T2DM and also achieved, after 6 months, a major fall of mean HbA_{1c} in the control group, from 8.1 to 7.2% compared to a slightly but significantly greater drop from 8.1 to 7.0% in the intervention group [19]. These results support the conclusion that rapid and major improvement of glycaemic control due to initiation or aggressive use of anti-diabetic treatment may limit the contribution of SMBG to the disease management.

The German-Austrian trial [22] used SMBG as a tool of patient empowerment for self-management. Instructing and training of patients and medical personnel in the proper performance and interpretation of SMBG data therefore required more interactions than in the control group. Both groups had improved mean HbA_{1c} levels, which was significantly better in the SMBG group (decrease by 1.0 vs 0.54%). This trial demonstrates the better outcome with intense counselling but it cannot disentangle the contribution of SMBG from other components of patient care.

The DiGEM trial concluded that there was no impact of SMBG in a large study of 12 months duration [18] with the SMBG-guided disease management protocol employed failing to make a difference. One possible explanation is that it is difficult to further improve glycaemia in patients with fairly well-controlled diabetes (mean HbA_{1c} 7.5%).

Improved HbA_{1c} levels in the group using SMBG (and to some degree also in control groups), were reported in trials with mean baseline HbA_{1c} levels of ≥ 8% [21;22;33;35]. This led to the concept of a 'floor effect' for the contribution of SMBG to metabolic control, i.e. little improvement in patients with HbA_{1c} values around 7.5%.

Despite the varying outcomes, these RCTs [18-20;22;33] allow several tentative conclusions:

1. SMBG may promote better glycaemia in non-insulin-treated T2DM but only if implemented together with training that includes learning how to adjust diet and lifestyle based on the results, as was the case in the German-Austrian trial.
2. In periods of rapid intensification of medication, SMBG per se has no apparent additional impact (King Drew Medical Center, ESMON trial) or only limited impact (DINAMIC-1 trial) on glycaemic control.
3. SMBG has little effect in people with stable, near-target metabolic control (HbA1c level around 7.5%) (DiGEM trial).

Studies of costs and cost-effectiveness of SMBG

Evidence-based economic considerations are an integral part of optimizing the use of healthcare resources and recommending specific healthcare strategies. However, despite the high usage and cost of SMBG procedures, there is scarce information on their cost-effectiveness.

An analysis by Simon and colleagues [36] assessed the cost-effectiveness of SMBG in type 2 subjects who participated in the DiGEM study [18] discussed earlier. The average annual cost of intervention was £89 (€113; $179) for standardized usual care, £181 for less intensive self-monitoring, and £173 for more intensive self-monitoring, showing an additional cost per patient of £92 (95% confidence interval £80 to £103) in the less intensive group and £84 (£73 to £96) in the more intensive group. Given that there were no significant differences in clinical outcomes (change in HbA_{1c}), the authors concluded that SMBG is unlikely to be cost-effective when additional to standardized usual care.

The Veterans Affairs (VA) guidelines now recommend that persons with stable T2DM treated with oral glucose-lowering drugs (OGLD) or diet-only therapy should perform SMBG twice weekly [37]. To measure the impact of such a recommendation on costs and metabolic control (HbA_{1c} levels), investigators used a retrospective, non-crossover clinical trial. The subjects' baseline average SMBG frequency and HbA_{1c} were compared with those obtained during a 6-month period, 2 months after implementation of the mentioned guidelines. At baseline, SMBG users treated with OGLD had mean (±SEM) HbA_{1c} values of 7.83 ± 1.34%

and a SMBG frequency of 1.36 ± 0.95 strips/patient/day. After guidelines implementation, the frequency of SMBG decreased by 46% (0.74 ± 0.50 strips/patient/day; p<0.0001) and their HbA_{1c} remained stable at 7.86 ± 1.54%; (p=0.63 vs baseline) although remaining well above the established target HbA_{1c} of 7.0%. SMBG users on diet therapy had baseline HbA_{1c} values of 6.85 ± 0.97% and a SMBG frequency of 1.07 ± 0.90 strips/patient/day. Post-implementation the frequency of SMBG fell by 35% (0.70 ± 0.51 strips/patient/day (p<0.0001) and their HbA_{1c} remained essentially unchanged at 6.78 ± 1.20%; NS vs baseline). Average monthly cost savings were US$ 8,800 or US$ 6.37/patient/month. The authors concluded that under their conditions the decrease in the frequency of SMBG in persons with T2DM resulted in a substantial cost savings, without adversely affecting overall control.

Conversely, a Kaiser Permanente study (USA) showed improvement in HbA_{1c} related to frequency of SMBG in people with T2DM treated with OGLD [38], Tunis and colleagues [38] estimated the cost-effectiveness of SMBG using a validated model projected clinical and economic outcomes for SMBG frequency of 1 or 3 times per day vs no SMBG over a 40-year period. Their results showed an increase in quality-adjusted life-years (QALYs) of 0.103 and 0.327 respectively. Corresponding incremental cost-effective ratios (ICERs) were US$ 7,856 and US$ 6,601 per QALY. These results indicate that SMBG at both 1 and 3 times per day in this cohort of people with T2DM treated with OGLD represents good value for money (USA), with ICERs being most sensitive to the time horizon; however, these findings remain controversial [39].

Palmer and colleagues [40] performed a similar study using the Markov/Monte Carlo modelling simulating the progression of macro/microangiopathic complications. The transition probabilities and HbA_{1c}-dependent adjustments used in this study came from the UKPDS and other major studies while effects of SMBG on HbA_{1c} levels came from clinical studies, meta-analyses and population studies. They found that depending on the type of diabetes treatment (diet and exercise, oral medications, insulin), improvements in glycaemic control with SMBG improved discounted QALYs anywhere from 0.165 to 0.255 years. Total treatment costs were £1,013 to £2,564 per patient with incremental cost-effectiveness ratios of £4,508 and £15,515 per QALY gained. The authors conclude that based on the moderate level of clinical evidence available, improvements in glycaemic control with interventions such as SMBG can improve patient outcomes with acceptable cost-effectiveness in a UK setting.

Weber and colleagues [41] used the ROSSO trial data set for an analysis of SMBG cost-effectiveness by considering total costs of diabetes and complications observed during 8 years (matched pair analysis). In patients treated with OGLD, costs of SMBG (strips, lancets, devices) were less than 2% of total treatment costs. Treatment costs were lower (by CHF 514) with SMBG use compared with non-SMBG use. In those people treated with OGLD plus insulin, the cost reduction was even greater (by CHF 3,522).

In many countries, a key issue facing individuals with diabetes (and their healthcare providers) is obtaining

reimbursement for SMBG supplies. Although a cost–benefit ratio for SMBG use has yet to be determined, the absence of or inadequate reimbursement for SMBG supplies has been linked to reduced SMBG use and consequently poorer glycaemic control among lower-income individuals. For example, Bowker and colleagues [42] examined the effect of paying for SMBG supplies on glycaemic control using baseline survey data and laboratory data from 405 patients who were currently enrolled in a randomized controlled trial. They found that patients with insurance coverage for SMBG supplies had significantly lower HbA_{1c} concentrations than those without insurance coverage (7.1% vs 7.4%, p=0.03). In multivariate analyses that controlled for potential confounders, lack of insurance coverage for SMBG supplies was significantly associated with higher HbA_{1c} concentrations (adjusted difference 0.5%, p=0.006). These findings are consistent with an earlier report from Karter and colleagues [43] who found that SMBG practice patterns may be sensitive to out-of-pocket expenditures for SMBG testing strips, especially for those with lower incomes enrolled in a large managed care organization.

5. Assessment of study limitations

Reduced external validity

Strong patient preferences in non-blinded studies can threaten the observational external validity of SMBG trials. For example, if subjects are randomized to the non-preferred study arm, this may prompt 'resentful demoralization' which can worsen outcomes due to either non-adherence or negative placebo-like effect. Moreover, this may prompt patients to cross over to the other preferred study arm [44].

Periods of rapid improvement of glycaemic control, for example after initiation of antidiabetic therapy or during rapid and aggressive intensification of medication, may also overshadow a possible SMBG effect. Additionally, it may not be reasonable to expect substantive improvements in HbA_{1c} if subjects are already reasonably well-controlled or are near target HbA_{1c} levels.

External validity is also influenced by the attitudes and past experiences of the study subjects. Studies that include only former or very low-intensity SMBG users, while excluding higher-intensity users (at baseline), may preferentially select subjects who previously found SMBG of little or no benefit.

Subject contamination

Because the use of SMBG is an intervention reliant on behaviour, studies using double-blinded trial designs are not appropriate because the subject, and in most cases the investigator, will know to which group the intervention (SMBG) has been assigned. Further, unblinded, randomized, clinical trials may result in 'contamination' of control subjects who overhear information about an 'optimal' intervention (e.g. SMBG) at the trial site and then initiate their own management. The investigator may also inadvertently express enthusiasm for an intervention, again leading to the adoption of the experimental intervention among the control subjects. Consequently, in both situations, 'control' subjects may achieve better outcomes than if they had not been influenced. Clinical trials that use 'cluster randomization' – randomization by site rather than by subject – may be less likely to result in subject contamination [45].

Attrition bias and analytic approach

Intention-to-treat analysis with imputed missing values may be misleading in view of substantial non-adherence to self-monitoring in the SMBG arm in many RCTs. Per-protocol analysis describes outcome only in those patients adherent to protocol. This provides an adjunct to the intention-to-treat analysis when trying to evaluate the SMBG effect, but in general has not been presented. However, the resulting bias introduced by analysing only partially randomized cohorts must be considered.

Potential design constraints

When effect size differs significantly and substantively across subgroups ('effect modification'), analyses must be stratified appropriately. Previous studies have shown the benefits of SMBG differ for prevalent vs new SMBG users [28]. Other potential effect modifiers include lifestyle only vs pharmacologically treated; and poorly controlled vs well-controlled.

Another potential design constraint is insufficient intervention; i.e. SMBG that is either too infrequent or lacking concomitant behavioural education (lifestyle changes and treatment adjustments guided by SMBG data) which will limit expected effects. The limited adjunct counselling in the ESMON [33] trial may well explain why SMBG led to distress, in contrast to the German-Austrian [22] trial which showed that SMBG improved general well-being and reduced depressive symptoms when employing adjunct counselling. Many studies have not documented consistent meeting of healthcare team and patient to follow up, review and refine the suggested lifestyle and other treatment adjustments. Initial education alone may not be adequate. Inadequate duration of the trial can also affect outcomes involving behavioural changes. Short-duration studies may not provide enough time for subjects to change entrenched behaviours.

'Study effect' in behaviour-dependent intervention trials

Because SMBG relies on behaviour, one inherent limitation of RCTs is that participation per se has an impact on behaviour, at the level of participants as well as medical personnel/providers. This study effect alone (Hawthorne effect) can lead to an improvement of metabolic control as has previously been observed [46;47] and also seen in most studies discussed above. The study effect caused by the increased attention, motivation and empowerment pre-empts some of the effects associated with the use of SMBG. This renders the translation of RCT results into clinical practice more difficult than in trials of pharmacological intervention.

To date, randomized controlled trials of SMBG in non-insulin-treated T2DM were not designed in a way that would allow SMBG-guided self-management and patient care to be effective in improving metabolic control. Thus, for the purpose of designing appropriate randomized controlled trials of SMBG-guided diabetes management, it is important to consider their limitations when assessing the value of SMBG which is the use of a diagnostic measure for modifying patient behaviour and therapeutic decisions by doctors.

6. Future SMBG studies and study design

Reduced external validity

In order to more accurately determine the value of SMBG in promoting and guiding self-management as well as patient care by the provider, it must be integrated into a treatment protocol algorithm and guidelines for patient education. Training on how to respond to blood glucose data, by appropriate modification of medication (with or without an active role of the patient), is an essential requirement as well as support by the provider. Quite different protocols of effective disease management are conceivable, although the best study design to determine the value of SMBG does not exist at present. However, some general guidelines for RCTs to evaluate the role and benefit of SMBG can be designed based on the points discussed above and which are depicted in Table 2. A recent consensus report by the Coalition for Clinical Research – Self-Monitoring of Blood Glucose (CCR-SMBG) provides a detailed discussion of SMBG trial design [45]. As SMBG can be a component of many different strategies in the management of the person with T2DM, it is important to study the many different aspects of using SMBG in the broad spectrum of diabetes patient care.

7. Potential uses of SMBG

Although it is virtually impossible to fully separate SMBG from other components of diabetes management, the effective use of SMBG has several potential benefits in both diabetes education and treatment, providing:

- support to enhance a diabetes care programme that aims to educate people about their condition,
- an instrument for objective feedback on the impact of daily lifestyle habits, special situations (illness, stress) and medication on glucose levels, and thereby to foster self-management and empower the individual to make the necessary changes, and
- support to the healthcare team in providing individually tailored advice about lifestyle components and blood glucose-lowering medication.

Figure 1 illustrates how SMBG can serve a dual purpose to enhance diabetes education/`understanding and provide a tool for glycaemic assessment. Through this, SMBG use can promote self-confidence and facilitate the necessary behavioural changes and optimization of therapy and its consequent positive outcomes.

An essential component of this model is close collaboration between people with diabetes and their healthcare team, using SMBG as a means of working together to achieve the desired benefits, which include improved metabolic and clinical outcomes (improved safety and prevention of acute and chronic complications), resulting in improved quality of life and an improved economic outcome (or improved value, defined as health outcomes per cost) for both the person with diabetes and the healthcare system.

Diabetes education and understanding

Active and effective participation of people with diabetes in the control and treatment of their disease is an essential component of good diabetes care. For that purpose, it is necessary that people with diabetes have an adequate level of appropriate knowledge and skills relevant to making informed decisions for self-directed behaviour change and treatment adjustments, thereby enabling self-management to be integrated into their daily lives [48]. People with diabetes can gain the necessary knowledge, skills and motivation to modify, adopt and maintain healthy behaviours and positive attitudes toward self-management through a continuous education programme. Within this context, SMBG is a practical tool that can help people with diabetes to understand their disease; in particular, the influence of life events (exercise, meals, physical and emotional stress, etc) and glucose-lowering medication on their glycaemic status, well-being and quality of life.

Behavioural changes

Promoting and facilitating positive self-care behaviour is the prime purpose of diabetes self-management education and training (DSMT, DSME/T) [49]. A key benefit of SMBG is that it provides immediate feedback to users. Thus, SMBG has the potential to actively involve people in the control of their diabetes milieu through improved problem-solving and decision-making skills which also applies to their healthcare providers. There is good evidence that programmes which focus on self-management and emphasize behavioural strategies lead to better clinical outcomes in diabetes and other chronic diseases [50-54].

Glycaemic assessment

Currently, only invasive procedures such as SMBG and continuous glucose monitoring (CGM) are able to provide accurate information on the daily profile of blood glucose levels. The magnitude of glucose excursions has been shown to be the most reliable identifier of an increased risk of hypoglycaemia in the short term [55]. It has also been associated with micro- or macrovascular complications in the long term [56-59]. Therefore, it is of advantage that people with diabetes recognize the need (and are able) to respond appropriately to glucose excursions outside the normal range. The IDF and major diabetes societies have therefore recommended upper limits for postprandial glycaemia along with targets for fasting blood glucose and HbA_{1c} levels (Table 3) [60;61].

Optimization of therapy

Surprisingly, study protocols of most trials of SMBG in T2DM fail to incorporate the use of SMBG data by the healthcare team for aiding therapeutic decisions (34). However, a recent study by Barnett and colleagues showed a significant reduction in HbA1c levels in patients who used SMBG to adjust medication dosages (19). Comparisons have also been performed in diabetic pregnancy, with significantly better clinical outcome when postprandial blood glucose values were used as one target of glucose-lowering therapy (62;63). One potential use of SMBG is therefore the optimization of anti-diabetic therapy in addition to suggestions concerning its use to introduce necessary changes of daily lifestyle habits. It can also provide information about treatment adherence.

8. Recommendations

Although further studies are needed to more comprehensively assess the benefits, optimal use and cost-effectiveness of SMBG, the following recommendations have been constructed to guide people with non-insulin-treated T2DM, their healthcare providers and payers in the use of SMBG. Additional scientific evidence available in the future may necessitate a review of these current proposals.

Explanation and rationale

1. SMBG should be used only when individuals with diabetes (and/or their care-givers) and/or their healthcare providers have the knowledge, skills and willingness to incorporate SMBG monitoring and therapy adjustment into their diabetes care plan in order to attain agreed treatment goals.

Maintenance of blood glucose at levels that prevent the development and progression of chronic complications involves an appropriate balance between food intake, physical activity and drug therapy, continuously adapting to the progressive metabolic changes inherent in diabetes. Achieving this balance requires the active and effective participation of people with diabetes, as well as of their healthcare providers, in the control and treatment of their disease. This requires the willingness and ability to make appropriate modifications to lifestyle and adjustments of medication and other treatment components according to daily blood glucose profiles. For this purpose, early use of SMBG may accustom individuals to diabetes self-management within a structured education framework.

In addition, use of SMBG can guide healthcare providers to identify and address specific blood glucose excursions (high and low) on a more timely basis. Often healthcare providers fail to initiate or intensify therapy appropriately during contacts/visits to

individuals with diabetes [64]. Such clinical inertia has been shown to contribute to poor glycaemic control in people with T2DM who are managed in primary care settings [65] and academic medical centres [66].

2. SMBG should be considered at the time of diagnosis to enhance the understanding of diabetes as part of individuals' education and to facilitate timely treatment initiation and titration optimization.

SMBG can be used as a way to teach people with diabetes about their disease and physiological responses to external stimuli. Despite inconsistent findings from RCTs and observational studies, SMBG can be useful as part of a comprehensive education programme that empowers both people with diabetes and members of the healthcare team to adjust treatment and behaviours based on SMBG results [22;24;67;68]. Because T2DM is a progressive disease that often requires ongoing assessment and adjustment of the treatment regimen, repeated educational sessions about appropriate SMBG use are necessary. It is critical that the design of educational programmes considers the initial educational and health literacy level of their attendants and ensure that the practical use of SMBG is clearly understood as well as ensuring the competence of the individual on an ongoing basis.

3. 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 pharmacological interventions as needed, in consultation with their healthcare provider.

It is critical that people with diabetes and/or their healthcare providers are willing and able to use SMBG appropriately and effectively. SMBG should be used only when the following criteria are met in the person with diabetes or the healthcare provider, or both.

People with diabetes:

- possess the knowledge and skill to accurately perform SMBG and record their test results and related events (manually or electronically), and
- possess the knowledge and ability to accurately interpret their test results to identify acute and chronic issues with glycaemic control and make appropriate adjustments to their lifestyle, e.g. in their meal plan, exercise regimens and also their drug treatment plan as required.

Healthcare providers:

- ensure the competence of the individual in carrying out SMBG on an ongoing basis,
- possess the knowledge, ability and willingness to consistently review SMBG results and make appropriate treatment adjustments (behavioural and pharmacological) as needed,
- are willing to document that they have reviewed patients' SMBG data (log book or electronic) on a regular basis and have used the data in their therapeutic plan related to glycaemic control, and
- use therapies that adequately address all abnormalities in parameters of daily glycaemic control (fasting/preprandial and postprandial glucose).

SMBG should be discouraged when it is not linked to diabetes self-management education and training and/or used to implement lifestyle or therapeutic changes.

4. SMBG protocols (intensity and frequency) should be individualized to address each individual's specific educational/behavioural/clinical requirements (to identify/prevent/manage acute hyper- and hypoglycaemia) and provider requirements for data on glycaemic patterns and to monitor impact of therapeutic decision making.

Given the significant diversity of clinical status, treatment regimens, educational needs and socio-economic issues within the non-insulin-treated T2DM population, effective use of SMBG requires that testing regimens be individualized to address the specific needs of each person with diabetes.

Although we currently have no evidence base regarding optimal SMBG regimens in non-insulin-treated T2DM, it is generally agreed that it is often not necessary to perform SMBG on a daily basis in this population. We suggest below some possible SMBG regimens for consideration, but emphasize that SMBG recommendations should be based on shared decision making by the patient and provider. It may be valuable for people with diabetes to perform 'focused' SMBG over short periods of time, initially and periodically, during the course of their disease, in order to obtain data that facilitate identification of glucose patterns that are reflective of daily glycaemic control [60;69].

For example, a 5-point or 7-point SMBG regimen, testing blood glucose before and after each meal and at bedtime over the course of 1 to 3 days, may be used to create a representative glucose profile. Alternatively, a 'staggered' regimen can be used to obtain blood glucose levels before and after alternating meals over a 2 to 3-week period [70;71]. **Figure 2** presents some suggested focused testing regimens to consider.

There are several situations in which short-term focused SMBG may be beneficial to people with non-insulin-treated T2DM. These include times when individuals [60;69]:

- have symptoms of hypoglycaemia,
- have infections, are travelling or are under stress,
- are undergoing adjustments in medication, nutrition and/or physical activity,
- are entering a new life experience, such as going away to school, starting a new job or changing work hours,
- are experiencing worsening HbA_{1c} values,
- are unclear or require additional information about the nature of their disease and/or the impact of their treatment (non-pharmacological and pharmacological) on their glucose control, or
- are pregnant or planning to become pregnant.

After sufficient glucose profiles have been obtained and addressed, it would therefore be reasonable to review the SMBG frequency and intensity. SMBG could be reduced to performing pre- and postprandial testing 2 to 3 times per week as a way to monitor glucose control and identify problems as they emerge. Also, periods of no SMBG could be prolonged if there is stable and 'good' metabolic control. **Figure 3** presents some suggested low-intensity SMBG regimens to consider. However, in situations where an individual wants to introduce a new meal plan or exercise regimen into his/her diabetes management, SMBG could be useful even if glucose control is stable.

A recent review by Gerich and colleagues showed that meal-based SMBG, when used as part of a comprehensive treatment regimen, is valuable in helping people with diabetes understand the impact of their nutritional intake, physical activity and medications on glucose levels, resulting in improved glycaemic control [72]. Meal-based SMBG can also be of help to clinicians in order to identify postprandial hyperglycaemia, guide therapeutic adjustments and receive more timely feedback regarding medication changes [72].

5. The purpose(s) of performing SMBG and using SMBG data 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.

Interaction between individuals with diabetes and healthcare providers is critical for the achievement of treatment goals [73]. Thus, SMBG use by people with T2DM should be based on shared decision making between the person with diabetes and the health provider. Within this context, the purpose of using SMBG should be clearly defined and agreed upon by both the person with diabetes and his/her healthcare provider. It is important for patient and provider to agree on glucose targets before and after meals and one commonly taught principle of assessing SMBG is that if 50% of an individual's glucose readings are within the targets established (assuming fairly standard targets) this will usually result in the A1c also being within an acceptable target [74].

It is essential that people using SMBG be given clear instructions regarding their role in making lifestyle and therapeutic adjustments based upon their SMBG data. Instructions should be provided as part of the diabetes education programme early in the course of the disease and reinforced at subsequent clinic visits. Moreover, it is critical that providers discuss cost implications and consider economic barriers that may be present for their patients, especially if the out-of-pocket cost of test strips reduces the patient's ability to pay for their glucose-lowering or other important therapies.

6. SMBG use requires an easy procedure for patients to regularly monitor the performance and accuracy of their glucose meter.

An important aspect of ongoing diabetes education is ensuring the quality of SMBG results. This is especially critical at the lower end of the glucose range [75;76]. Quality control of SMBG is recommended as a routine procedure in diabetes management [77]. The quality assurance procedure should be easily accessible to patients and provide a convenient, not time-consuming, reliable assessment of glucose meter performance [77]. Optimally, assessment of both quality control checks and patient testing technique should be performed periodically in the diabetes outpatient clinic and performed by a trained nurse or a diabetes educator [78]. People with diabetes should be given advice regarding whom to contact in the event of a problem with their blood glucose meter.

Additionally, industry has a responsibility to continue to produce blood glucose monitoring systems that yield accurate and reliable test results. This will require ongoing efforts to further improve accuracy and develop new technologies that reduce the effects of substances that would interfere with accurate readings.

Cost implications

Given the relatively high cost of SMBG, particularly the ongoing use of test strips, it would be remiss to ignore the economic implications of the suggested recommendations above. Where patients have to pay out-of-pocket expenses for medical supplies, financial barriers have been shown to reduce use of SMBG [43;79;80]. The potential benefits of SMBG must therefore be balanced against its cost, especially when such expenditure may come at the expense of other treatment modalities (e.g. medication, staff, facilities, and others). This is particularly important in developing nations. Use of visually read test strips does provide a lower-cost alternative to meter/test strip SMBG systems; however, this method has potentially significant limitations in terms of accuracy of data interpretation and collection. The commercial sector is urged to develop a low-cost, high-quality option that can be made available everywhere in the future.

9. Summary

Diabetes is a significant and growing worldwide concern with potentially devastating consequences [1]. Numerous studies have demonstrated that optimal management of glycaemia and other cardiovascular risk factors can reduce the risk of development and progression of both microvascular and macrovascular complications [3-6;8-12;16].

Results from studies of SMBG use in non-insulin-treated T2DM have been mixed, due to differences in study design, populations, outcome indicators, and inherent limitations of the traditional RCT models used. However, current evidence suggests that using SMBG in this population has the potential to improve glycaemic control, especially when incorporated into a comprehensive and ongoing education programme that promotes management adjustments according to the ensuing blood glucose values [22;67;68].

SMBG use should be based on shared decision making between people with diabetes and their healthcare providers and linked to a clear set of instructions on actions to be taken based upon SMBG results. SMBG prescription is discouraged in the absence of relevant education and/or ability to modify behaviour or therapy modalities.

In summary, the appropriate use of SMBG by people with non-insulin-treated diabetes has the potential to optimize diabetes management through timely treatment adjustments based on SMBG results and improve both clinical outcomes and quality of life. However, the value and utility of SMBG may evolve within a preventive care model that is based on ongoing monitoring and the ability to adjust management as the diabetes progresses over time. In the meantime, more effective patient and provider training around the use of SMBG is needed. Because skilled healthcare professionals are needed now and in the future to address the growing diabetes epidemic, it is hoped that this report will encourage the development and systematic introduction of more effective diabetes self-management education/training and the value-based models of clinical decision making and care delivery.

Table 1A. Summary of key observational studies

Study	Description of purpose	Findings/comments
Fremantle Diabetes Study[31]	■ Assessed whether SMBG is an independent predictor of improved outcome in a community-based cohort of T2DM patients ■ Used longitudinal data from 1,280 T2DM participants (70% ongoing SMBG users at baseline) and a subset of 531 individuals who attended annual assessments over a 5-year period	■ SMBG was associated with a 48% decreased risk of cardiovascular mortality in insulin-treated patients, but a 79% increased risk in non-insulin-treated patients ■ Time-dependent SMBG was independently associated with a 48% reduced risk of retinopathy in the 5-year cohort *'Inconsistent findings relating to the association of SMBG with cardiac death and retinopathy may be due to confounding, incomplete covariate adjustment or chance'*
Kaiser Permanente[28]	■ Assessed longitudinal association between SMBG and glycaemic control in diabetic patients from an integrated health plan ■ Followed 16,091 new SMBG users and 15,347 ongoing users over a 4-year period	■ Greater SMBG frequency among new users was associated with a graded decrease in HbA_{1c} (relative to non-users) regardless of diabetes therapy ■ Longitudinal changes in SMBG frequency were related to significant changes in glycaemic control
QuED[29]	■ Assessed impact of SMBG on metabolic control in non-insulin-treated T2DM subjects (41% ongoing SMBG users at baseline) ■ Followed 1,896 patients over a 3-year period	■ Performance and frequency of SMBG did not predict better metabolic control over 3 years ■ Investigators could not identify any specific subgroups for whom SMBG practice was associated with lower HbA_{1c} levels during the study
ROSSO[30]	■ Investigated relationship of SMBG with disease-related morbidity and mortality ■ Followed 3,268 patients from diagnosis of T2DM between 1995 and 1999 until end of 2003 (mean follow-up 6.5 years) retrospectively from medical records	■ SMBG was associated with decreased diabetes-related severe morbidity and all-cause mortality ■ This association was also seen in subgroup of non-insulin-treated patients ■ Medical records contained data on some biochemical parameters, retinopathy and neuropathy for only a small proportion of patients

Table 1B. Summary of key randomized controlled trials

Study	Description of purpose	Findings/*comments*
King-Drew Medical Center Trial[20]	■ Randomized, single-blind study designed to determine whether SMBG improves HbA1c in non-insulin-treated T2DM patients ■ Clinical management decisions were blinded to SMBG data and use ■ 89 non-insulin-treated T2DM patients were followed for 6 months	■ At 6 months, differences in decrease in HbA1c levels were not statistically significant *The rapid upgrading of medication every two weeks if goals were not met may have obscured the potential of SMBG for supporting self-management*
ESMON[33]	■ Prospective randomized controlled trial assessed the effect of SMBG vs no monitoring on glycaemic control and psychological indices in patients with newly diagnosed T2DM ■ Evaluated 184 non-insulin-treated patients with no previous use of SMBG over 12 months	■ There were no significant differences in HbA_{1c} between groups at any time point ■ SMBG was associated with a 6% higher score on the depression subscale of the well-being questionnaire *The major improvement of mean HbA_{1c} levels in the control group, from 8.6 to 6.9% indicates a dominant role of medication in disease management*
DINAMIC[19]	■ Multicentre, randomized, parallel-group trial was designed to determine if therapeutic management programmes for T2DM that included SMBG result in greater reductions in HbA_{1c} compared with programmes without SMBG in non-insulin-treated patients ■ Followed 610 T2DM patients with early or mild diabetes receiving an identical oral anti-diabetic therapy regimen with gliclazide for 27 weeks	■ There was a major decrease of HbA_{1c} which was significantly larger in the SMBG group than the control group ■ The incidence of symptomatic hypoglycaemia was lower in the SMBG group *The major improvement of HbA_{1c} levels in the control group from 8.1 to 7.2% indicates a dominant role of medication in disease management*

Study	Description of purpose	Findings/comments
German-Austrian[22]	■ Prospective, multicenter, randomized controlled study Investigated the effect of meal-related SMBG on glycaemic control and well-being in non-insulin-treated T2DM subjects ■ Followed 250 non-insulin-treated T2DM patients for 6 months	■ In per-protocol analysis (n=223) use of SMBG significantly reduced HbA1c levels ■ SMBG use resulted in a marked improvement of general well-being with significant improvements in the subitems depression and lack of well-being *The benefit of intense patient care is evident but the contribution of intense vs SMBG cannot be assessed*
DiGEM[18]	■ Three-arm, open, parallel group randomized trial designed to determine whether SMBG alone, or with instruction in incorporating results into self-care, is more effective than standardized usual care in improving glycaemic control in non-insulin-treated T2DM patients ■ Followed 453 patients with a mean HbA_{1c} level of 7.5% for a median duration of 1 year.	■ At 12 months the differences in HbA_{1c} level between the three groups were not statistically significant ■ Investigators concluded that evidence is not convincing of an effect of SMBG, with or without instruction in incorporating findings into self-care, compared with usual care in reasonably well controlled non-insulin-treated patients with type 2 diabetes.

Table 2. Alternative experimental designs that address specific aspects of SMBG use for which additional evidence is needed

- Study protocols that focus on SMBG use as part of a diabetes educational strategy rather than being used only as an ongoing monitoring tool; its use should be linked to a clear set of instructions on action to be taken based on the SMBG results at the level of the patient (for changes of daily dietary and exercise habits, for adjustment of anti-diabetic medication) and/or at the level of medical personnel (providing advice on changes of daily habits, adjustment of medication).

- Trials that evaluate the efficacy of clinical training programmes for SMBG-guided, therapeutic decision making among various healthcare providers in various healthcare settings.

- Trials which incorporate interventions that are based upon recognized behavioural medicine conceptual frameworks in order to learn how to improve treatment adherence in people with diabetes. This includes the analysis of whether psychosocial characteristics and readiness to change could be used to predict and target those who actually make (and will benefit from) behavioural changes.

- 'Pragmatic trials' or 'practical trials' are sometimes useful to maximize external validity. Such designs measure the effectiveness of SMBG in real clinical practice rather than highly selected trial populations, while maintaining internal validity [81].

- All above trials can be used to determine cost-effectiveness by calculating SMBG costs versus differences in cost of medication between treatment groups and projected differences in clinical outcome as derived from the presence of established risk markers of complications such as HbA_{1c}, blood pressure, blood lipids and BMI (by using an established risk calculator program).

Table 3. Guidelines for glycaemic control in T2DM

	IDF [82;83]	AACE [60]	ADA [61]
HbA_{1c} (%)	<6.5	≤6.5	<7.0
Fasting/preprandial glucose (mmol/L / mg/dL)	<6.0 / <110	<6.0 / <110	3.9-7.2 / 70-130
2-h postprandial glucose (mmol/L / mg/dL)	<7.8 / <140	<7.8 / <140	<10.0 / <180*

*ADA recommends that postprandial glucose measurements should be made 1–2 h after the beginning of the meal.

SMBG as a Component of the Education/Treatment Programme

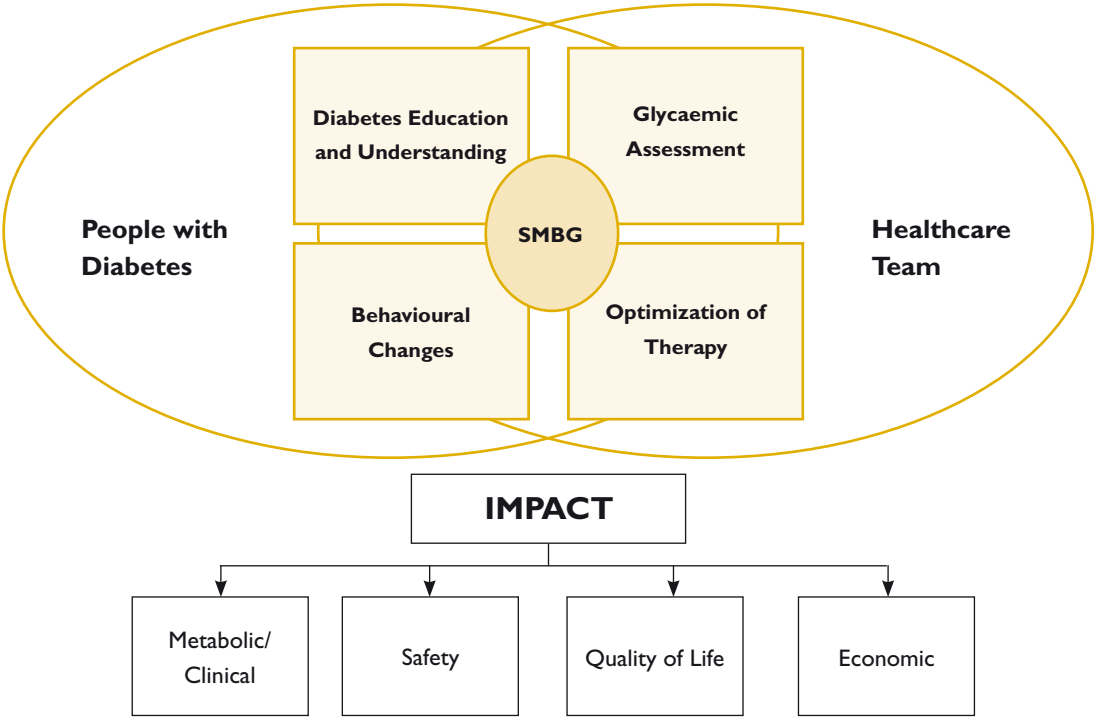

Figure 2. Examples of focused SMBG regimens

5-point profile

	Pre-Breakfast	Post-Breakfast	Pre-Lunch	Post-Lunch	Pre-Supper	Post-Supper	Bedtime
Monday							
Tuesday							
Wednesday	X	X		X	X	X	
Thursday	X	X		X	X	X	
Friday	X	X		X	X	X	
Saturday							
Sunday							

7-point profile

	Pre-Breakfast	Post-Breakfast	Pre-Lunch	Post-Lunch	Pre-Supper	Post-Supper	Bedtime
Monday							
Tuesday	X	X	X	X	X	X	X
Wednesday	X	X	X	X	X	X	X
Thursday	X	X	X	X	X	X	X
Friday							
Saturday							
Sunday							

'Staggered' SMBG regimen

	Pre-Breakfast	Post-Breakfast	Pre-Lunch	Post-Lunch	Pre-Supper	Post-Supper	Bedtime
Monday	X	X					
Tuesday			X	X			
Wednesday					X	X	
Thursday	X	X					
Friday			X	X			
Saturday					X	X	
Sunday	X	X					

Intensive or 'focused' SMBG protocols use 'pattern analysis', a systematic approach to creating glucose profiles that can identify daily glycaemic patterns and then take appropriate action based upon those results. These profiles can be generated by performing 5 to 7 measurements per day over 1 to 3 days, or through 'staggered' testing, in which the individual performs pre- and postprandial testing for alternating meals over the course of a week.

Figure 3. Examples of low-intensity SMBG regimens

Meal-based testing

	Pre-Breakfast	Post-Breakfast	Pre-Lunch	Post-Lunch	Pre-Supper	Post-Supper	Bedtime
Monday	X	X					
Tuesday							
Wednesday			X	X			
Thursday							
Friday							
Saturday					X	X	
Sunday							

Meal-based SMBG (before and after selected meals) helps individuals with diabetes understand the effects of their treatment on blood glucose concentrations and assists clinicians in identifying postprandial hyperglycaemia, guides therapeutic adjustments and provides more timely feedback regarding medication changes [72].

A more comprehensive approach, which has been used in early education programmes with good results (84), is to perform 3 tests per day (2 times per week – one weekday and one weekend day) – fasting and preprandial/postprandial at the largest meal (often supper) for a few weeks . Monitor fasting glucose to track trends in glucose control. Monitor preprandial/postprandial (largest meal first) during week and weekend for a few weeks and then change diet and exercise to optimize the result. Then monitor preprandial/postprandial glucose at another meal and repeat it.

Detection/assessment of fasting hyperglycaemia

	Pre-Breakfast	Post-Breakfast	Pre-Lunch	Post-Lunch	Pre-Supper	Post-Supper	Bedtime
Monday							X
Tuesday	X						
Wednesday							X
Thursday	X						
Friday							X
Saturday	X						
Sunday							

Bedtime and morning fasting SMBG can be used to identify fasting and assess fasting hyperglycaemia.

Detection of asymptomatic hypoglycaemia

	Pre-Breakfast	Post-Breakfast	Pre-Lunch	Post-Lunch	Pre-Supper	Post-Supper	Bedtime
Monday			X		X		
Tuesday							
Wednesday			X		X		
Thursday							
Friday			X		X		
Saturday							
Sunday							

Pre-lunch and pre-supper SMBG can be used to detect asymptomatic hypoglycaemia [85].

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