Internet Blood Glucose Monitoring Systems Provide Lasting Glycemic Benefit in Type 1 and 2 Diabetes

A Systematic Review

Hugh D. Tildesley, MD[a,*], Michelle D. Po, PhD[b], Stuart A. Ross, MD[c]

KEYWORDS

• Diabetes • Glycemic control • Hypoglycemia • Self-monitoring of blood glucose • Internet medicine • Internet blood glucose monitoring system

KEY POINTS

- Internet blood glucose monitoring systems (IBGMS) result in glycemic improvement in patients with type 1 or 2 diabetes, including those with poorly controlled glycemia at baseline.
- IBGMS help decrease glycemic levels without increasing the risk of hypoglycemia.
- Other benefits, seen in some studies of IBGMS, include improvements in cardiovascular risk markers and quality of life outcomes.
- Glycemic improvements with IBGMS are not limited to patients on insulin or to those who increase their frequency of glucose self-monitoring as a result of the intervention.
- Glycemic improvements likely result from a combination of factors, including increased patient motivation and increased communication between patient and health care provider.

INTRODUCTION

Effective glycemic control is associated with reduced risk of complications of type 1 diabetes (T1D) and type 2 diabetes (T2D).[1–4] In controlled clinical trials, even when

Disclosures: H.D. Tildesley uses Internet blood glucose monitoring routinely in managing patients with diabetes. M.D. Po and S.A. Ross declare that they have no financial or other competing interest in the topics discussed here.

[a] Department of Endocrinology and Metabolism, St Paul's Hospital, University of British Columbia, Room 410, 1033 Davie Street, Vancouver, British Columbia V6E 1M7, Canada; [b] SCRIPT, 2010 Yonge St, Toronto, ON M4N 2K4, Canada; [c] University of Calgary, 2500 University Dr NW, Calgary, AB T2N 1N4, Canada

* Corresponding author.

E-mail address: hdtildesley@gmail.com

Med Clin N Am 99 (2015) 17–33

http://dx.doi.org/10.1016/j.mcna.2014.08.019 **medical.theclinics.com**

the early glycemic control is lost at a later point, patients who establish and maintain good control early in the course of their disease may enjoy reduced risk of macrovascular and microvascular complications of diabetes over a period of years to decades.[3–5] For this reason, current treatment guidelines emphasize the need for timely introduction of lifestyle and, if necessary, pharmacologic interventions, to bring patients to appropriate glycemic targets within months of diagnosis.[6] Despite this guidance, and despite clear evidence that effective glycemic control can prevent diabetic complications, only half of North American patients achieve the standard glycemic target of hemoglobin A_{1c} (HbA_{1c}) level less than 7%.[7–9]

For patients with T1D and insulin-using patients with T2D, American Diabetes Association (ADA) and Canadian Diabetes Association (CDA) treatment guidelines support regular self-monitoring of blood glucose (SMBG), which allows the patient to titrate insulin doses, evaluate their success in reaching glycemic targets, and gauge their risk of hypoglycemia.[6,10] However, the clinical usefulness and cost-effectiveness of SMBG in controlling glycemic levels in non–insulin-using patient with T2D is less clear. A recent meta-analysis showed that regular SMBG in this patient population was associated with a statistically significant but quantitatively minor glycemic benefit.[11] Uncertainty about the role of SMBG outside the context of insulin dose adjustment is reflected in the 2014 ADA guidelines; these guidelines recommend SMBG as a part of a broader educational context, and to help guide treatment decisions for non–insulin-using, as well as insulin-using, patients.[10]

We have proposed elsewhere[12–14] that increased patient-physician communication, in the form of ongoing Internet-based contact, could increase the effectiveness of SMBG as a means to improve diabetes management in combination with regular care. In this article, a systematic review of Internet blood glucose monitoring systems (IBGMS) is provided, which facilitate regular health care provider review and feedback regarding a patient's SMBG results. In such systems (**Fig. 1**), patients carry out regular glucose monitoring and upload the resulting data to a secure Web site. From there, the data are reviewed by a health care professional, who provides feedback on the results, offers encouragement, and, as appropriate, recommends changes to the patient's monitoring practices, insulin titration, or diet.

In this article, the efficacy, safety and other outcomes are evaluated from numerous small studies comparing patients using IBGMS with other patients with more

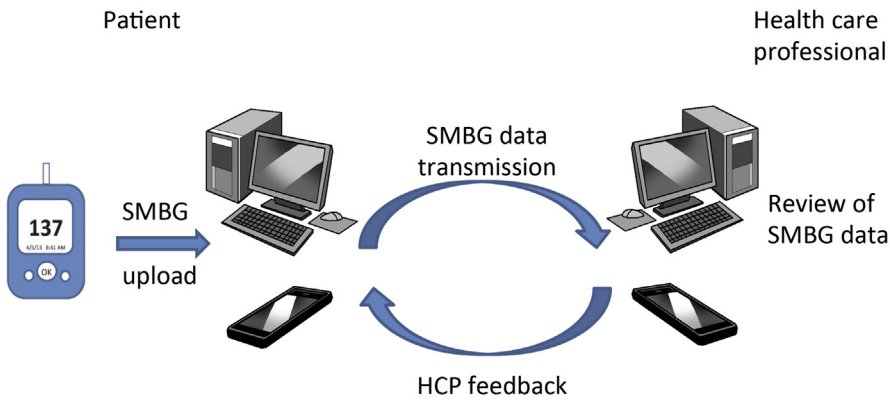

Fig. 1. IBGMs. All Internet-based interventions considered in this review include the following: (1) patient's SMBG, (2) uploading and transmitting the SMBG data to a health care professional (HCP), (3) the HCP reviewing and submitting feedback to the patient.

traditional patterns of physician contact. IBGMS is consistently associated with significant improvement in glycemic control, with no evident safety concerns. Several hypotheses to explain the benefits of this intervention in patients are then considered, with various treatment histories. The evidence is examined that, given the prevalence of personal computers and mobile devices in contemporary society, IBGMS offer a potentially cost-effective and time-sparing approach to diabetes management.

METHODS

We performed PubMed searches in March, 2014, using the following terms to find research articles reporting IBGMS trials: Internet + diabetes, Web-based + diabetes, telemedicine + diabetes, and telehealth + diabetes. Additional articles were chosen by examining the reference lists of relevant reviews. Forward searching using Web of Science identified works in which key articles were cited.

Publications on T1D or T2D were included in this analysis if they reported randomized controlled trials of standard practice versus IBGMS, which were defined as systems with 3 components: Web-based uploading of patients' SMBG data, regular review of the data by a health care professional, and digital or telephonic feedback. Studies were excluded if they included only adolescent patients or if they did not report HbA_{1c} as an outcome. No formal evaluation of levels of evidence was conducted.

SELF-MONITORING OF BLOOD GLUCOSE LEVELS ON INTERNET BLOOD GLUCOSE MONITORING SYSTEMS

It was anticipated that patients using IBGMS might monitor their glucose more frequently than other patients.

We identified 6 randomized controlled trials that reported SMBG frequency in both the IBGMS and control groups. In the 3 T1D studies identified,[15–17] there were no significant differences in SMBG frequency between patients in IBGMS and control groups. In the 3 T2D studies identified, patients on IBGMS self-monitored significantly more often than patients on conventional care: 55.7 times/mo versus 14.9 times/mo, $P<.001$,[18] 23.8 times/mo versus 12.7 times/mo, significance not reported[19] and 34 times/mo versus 22 times/mo, $P = .024$.[20]

SHORT-TERM AND LONGER-TERM GLYCEMIC CONTROL WITH INTERNET BLOOD GLUCOSE MONITORING SYSTEMS IN TYPE 2 DIABETES

We identified 9 randomized controlled IBGMS trials that enrolled type 2 patients and 4 studies that enrolled patients with either T1D or T2D (**Table 1**). All but 1 of these studies[21] showed significantly improved HbA_{1c} level in the IBGMS group compared with the control group, as seen either in a significant difference in glycosylated hemoglobin change (ΔHbA_{1c}) between groups or in a significant decrease in HbA_{1c} level in the IBGMS group but not the control group.

Of the 12 T2D studies, 7[18,20,22–26] enrolled 50% or more non–insulin-using patients, suggesting that IBGMS is effective in non-insulin-using patients. In the 1 study that failed to find a significant improvement in HbA_{1c} level with IBGMS in the total patient population, a subanalysis of non–insulin-using patients nevertheless showed a significant decline in HbA_{1c} level in the IBGMS group relative to controls: mean HbA_{1c} level decreased from 6.95% to 6.66% in the IBGMS group compared with 7.21% to 7.2% in the control group ($P = .02$). In 3 studies, some patients were treated with diet and exercise alone, with no pharmacotherapy for diabetes.[18,25,27] However, because these

Table 1
Randomized controlled studies of IBGMS versus conventional care: glycemic, cardiovascular risk, and quality of life outcomes

Study	Participants (Intervention vs Usual Care)	Treatments in Use	Duration (mo)	Description of IBGMS (Method of Upload; Review; Feedback)	Mean HbA_{1c} Levels in IBGMS, from Baseline to Follow-Up (%)	Mean HbA_{1c} Levels in Control Group, from Baseline to Follow-Up (%)	*P* Value, Δ HbA_{1c} Levels Between Groups	CVD Outcomes at Follow-Up in IBGMS Compared with Control Group	QOL at Follow-Up in IBGMS Compared with Control Group
T2D									
Shea et al,[25] 2009; Trief et al,[46] 2007	≥55, 352 vs 353	65% OHA alone, 14% insulin alone, 15% insulin + OHA, 5% diet alone	60	Home telemedicine unit; nurse managers (diabetologists consulted when needed); Web-based	7.43–7.09, NR	7.45–7.38, NR	<.001	Significant improvement in SBP, DBP	No significant difference in depression or diabetes distress
Stone et al,[28] 2010	64 vs 73	76% OHA, 79% insulin (breakdown of OHA alone and insulin alone not reported)	6	Wireless glucometer; nurse under supervision of an endocrinologist; phone	9.6–7.9	9.4–8.6	<.001	Significant improvement in LDL	
Ralston et al,[24] 2009	30 vs 35	Diet, OHAs or insulin (38% used insulin)	12	Web-based; diabetes case manager; e-mail	8.2–7.3, *P* = .01	7.9–8.1, NR	<.01	No significant CVD benefits identified	
Kim et al,[20] 2007	25 vs 26	67% OHA, 31% insulin	12	Web-based; diabetic educator or professor; text message	8.09–7.04, *P*<.05	7.59–7.70, NS	.011	No significant CVD benefits identified	
Cho et al,[18] 2006	40 vs 40	69% OHA, 12% insulin only, 10% OHA + insulin, 9% exercise/diet	30	Web-based; clinical investigator, daily; Web-based	7.7–6.7, *P*<.05	7.5–7.4, NS	.022	Significant improvement in triglycerides	

Kwon et al,[19] 2004	51 vs 50	NR	3	Web-based; endocrinology fellow; Web-based	7.59–6.94, *P*<.001	7.19–7.62, NR	<.05		
Tildesley et al,[14] 2010; Tildesley et al,[13] 2011	24 vs 23	Insulin	6	Web-based; endocrinologist; Web-based	8.8–7.6, *P*<.001	8.5–8.4, *P* = .51	<.05	Significant improvement in total cholesterol and LDL	
Kim et al,[22] 2008	Obese 18 vs16	68% OHA, 32% insulin	12	Web-based; diabetic educator or professor; both by phone and Web-based	8.16–6.67, *P*<.05	7.66–8.19, NS	NR		
Yoon and Kim,[26] 2008	25 vs 26	69% on OHA only, 31% insulin	12	Web-based; endocrinologist/ professor; text message	8.09–6.77, *P*<.05	7.59–8.4, *P*<.05	NR	No significant CVD benefits identified	
Bujnowska-Fedak et al,[21] 2011	50 vs 50	50% insulin, 50% noninsulin	6	Wireless glucometer; physician; phone	7.6–7.4, NR	7.6–7.4, NR	NS	No significant CVD benefits identified	No significant QOL differences
T1D and T2D									
Bond et al,[27] 2007; Bond et al,[41] 2010	≥60 y old 36 vs 31	49% insulin, 45% insulin + OHA, 6% diet and exercise	6	Web-based; nurse; e-mail or instant messaging	7.0–6.4, NR	7.1–7.0, NR	.01	Significant improvements in total cholesterol, HDL, SBP	Significant improvements in depression (CES-D), QOL (PAID)
Harno et al,[40] 2006	101 vs 74	NR	12	Glucometer; diabetes team; text message	7.8–7.3, NR	8.2–7.8, NR	<.05	Significant improvements in total cholesterol, LDL, TG, DBP	

(*continued on next page*)

Table 1
(*continued*)

Study	Participants (Intervention vs Usual Care)	Treatments in Use	Duration (mo)	Description of IBGMS (Method of Upload; Review; Feedback)	Mean HbA_{1c} Levels in IBGMS, from Baseline to Follow-Up (%)	Mean HbA_{1c} Levels in Control Group, from Baseline to Follow-Up (%)	*P* Value, Δ HbA_{1c} Levels Between Groups	CVD Outcomes at Follow-Up in IBGMS Compared with Control Group	QOL at Follow-Up in IBGMS Compared with Control Group
McMahon et al,[23] 2005	$HbA_{1c} \geq 9\%$ 52 vs 52	51% on OHA, 49% on insulin	12	Web-based; nurse, physician; Web-based	−1.6 reduction from baseline, *P*<.001	−1.2 reduction from baseline, *P*<.001	<.05	Significant improvements in HDL, TG, SBP	
Tjam et al,[29] 2006	34 vs 19	NR	12	Web-based; nurse; Web-based	6.7–6.5, *P* = .045	6.8–6.8, *P* = .88	NR		
T1D only									
Charpentier et al,[15] 2011	61 vs 59	Insulin	6	cell-phone; physician; phone; Additional: Diabeo Decision-support software	9.11–8.41, NR	8.91–9.1, NR	<.001		No significant differences by DQOL and Diabetes Health Profile
Kirwan et al,[30] 2013	36 vs 36	Insulin	6	Smartphone app; diabetes educator; text message	9.08–7.8, *P*<.001	8.47–8.58, NS	<.001		No significant differences by DQOL
Montori et al,[16] 2004	16 vs 16	Insulin	6	Direct upload from glucometer; nurse (supervised by endocrinologist; phone call)	9.1–7.8, NR	8.8–8.2, NR	.03		
Jansa et al,[36] 2006	16 vs 14	Insulin	12	Glucometer through phone line; nurse; phone (teleconsultations took the place of in-person visits)	8.4–7.6, *P* = .008	8.9–7.6, *P* = .001	NS		No significant differences by DQOL

Gomez et al,[47] 2002	10 (crossover design)	Insulin	14	PDA; physicians and nurses; PDA-based	8.4–7.9, NR	8.1–8.15, NR	.053		
Benhamou et al,[32] 2007	15 vs 15	Continuous subcutaneous insulin infusion	6	PDA/cell; investigator; text message	8.31–8.18, $P = .17$	8.22–8.34, $P = .33$	.097		Significant improvements in DQOL global score and DQOL satisfaction with life subscale
Rossi et al,[17] 2013	63 vs 64	Insulin	6	Cell phone; physician; text message; Additional: automatic dosage calculation based on carb intake	8.4–7.9, <.0001	8.4–7.9, <.0001	.73	No significant CVD benefits identified	Significant improvements in perceived frequency of hyperglycemic episodes on DTSQ and social relations on DQOL
McCarrier et al,[48] 2009	25 vs 16	Insulin	12	Web-based; nurse; e-mail	7.99–7.62, NS	8.05–8.16, NS	.16		
Biermann et al,[35] 2002	27 vs 16	Insulin	8	Web-based; physician; phone (teleconsultations took the place of in-person visits)	8.3–7.1, NR	8.0–6.8, NR	NS		

Abbreviations: CES-D, Centre for Epidemiological Studies Depression scale; CVD, cardiovascular disease; DBP, diastolic blood pressure; DQOL, diabetes-specific quality of life questionnaire; DTSQ, diabetes treatment satisfaction questionnaire; HDL, high-density lipoprotein; LDL, low-density lipoprotein; NR, not reported; NS, nonsignificant; OHA, oral hypoglycemic agent; PAID, problem areas in diabetes; PDA, personal digital assistant (a small handheld computer); QOL, quality of life; SBP, systolic blood pressure; TG, triglycerides.

patients represented a small proportion of the study populations (~7–9%), and no subgroup analyses were performed, the effectiveness of IBGMS in patients relying on lifestyle modification alone to control their T2D cannot be evaluated.

Most studies were short, with follow-up between 3 and 12 months. Significant reductions in HbA_{1c} level with IBGMS were observed in as little as 3 months.[14,19,22,23,26] Two longer-term studies showed that the glycemic benefit of IBGMS can be maintained over several years. Cho and colleagues[18] reported that intervention patients experienced a decrease in HbA_{1c} level from a mean of 7.7% to 6.7% ($P<.05$) after 30 months, compared with 7.5% to 7.4% (not significant) in controls. The large-scale The Informatics for Diabetes Education and Telemedicine (IDEATel) trial also showed that IBGMS can deliver long-term glycemic benefit. After a 5-year follow-up, patients in the Internet intervention arm showed a mean decrease in HbA_{1c} level from 7.43% to 7.09%, compared with 7.45% to 7.38% in the conventional care arm; the change from baseline was significantly different between groups.[25] Both these studies had 70% to 78% non–insulin-using patients, suggesting that IBGMS can facilitate long-term glycemic control in individuals with T2D, independent of any benefits related to insulin dose titration.

Although these studies showed significant decline in HbA_{1c} level within 3 months of IBGMS use, this short-term intervention may not be sufficient to effect lasting glycemic control. Tildesley and colleagues[13] reported that mean HbA_{1c} levels in insulin-using patients with T2D decreased significantly, from 8.8% to 7.6% ($P<.001$) after a 6-month follow-up. However, after patients in the intervention group were returned to conventional care, HbA_{1c} levels returned to baseline within 6 months. Thus, ongoing patient-physician communication may be required to maintain the benefits of IBGMS.

INTERNET BLOOD GLUCOSE MONITORING SYSTEMS IN WELL AND POORLY CONTROLLED TYPE 2 DIABETES

Studies focusing on patients with higher HbA_{1c} level at baseline have shown some of the most remarkable improvements in glycemic control with IBGMS. Of 6 T2D studies featuring mean baseline HbA_{1c} level 8% or greater (1 with insulin only[14]; 5 with oral agents with or without insulin[20,22–24,28]), the mean decrease in HbA_{1c} level ranged from 1.05% to 1.7%, with the largest decrease seen in the study with the highest baseline HbA_{1c} level.[28]

In addition, patients with T2D who are at or near their glycemic target seem to maintain or improve their degree of glycemic control with IBGMS. Thus, in a study of both T1D and T2D, with patients on a variety of therapies, mean HbA_{1c} level declined from 7.0% to 6.4% in the Internet intervention group, whereas the control group HbA_{1c} level declined nonsignificantly from 7.1% to 7.0%.[27] Two studies that carried out a subanalysis of patients with baseline HbA_{1c} level less than 7.0% both showed a significant difference between intervention and control groups with regard to follow-up HbA_{1c} level.[18,19] Moreover, in the IBGMS study with the best glycemic control at baseline, HbA_{1c} level decreased significantly from a mean of 6.7% to 6.5% ($P = .045$) in the IBGMS group, versus 6.8% to 6.8% (not significant) in the control group.[29] Hence, baseline glycemic control does not seem to be a limitation in patient selection for IBGMS.

INTERNET BLOOD GLUCOSE MONITORING SYSTEMS IN WELL AND POORLY CONTROLLED TYPE 1 DIABETES

Although Internet interventions in T1D do not result in the same widespread improvement as seen in T2D studies, IBGMS result in a consistent trend toward greater

HbA_{1c} level reduction. This improvement reached statistical significance in some T1D trials, namely those in which patients experienced poor glycemic control at baseline.

Of the 9 identified trials of T1D, 3 showed a glycemic benefit for IBGMS compared with conventional care.[15,16,30] All of the studies that showed a significant glycemic benefit in the intervention arm had a mean baseline HbA_{1c} level of 8.4% or greater, whereas all the studies that failed to show a significant benefit of IBGMS use had a mean baseline HbA_{1c} level of 8.4% or less. As in comparable studies in T2D, greater change in HbA_{1c} level with IBGMS occurs in patients with poorly controlled disease.

HYPOGLYCEMIA AND INTERNET BLOOD GLUCOSE MONITORING SYSTEMS

Insulin and some oral agents decrease glycemic exposure at the cost of heightening patients' risk of overall and serious hypoglycemia.[1,2] This dose-limiting toxicity is important clinically, because of the intrinsic adverse effects of hypoglycemia, and also because of its psychological effect, whereby fear of hypoglycemia delays treatment implementation and reduces treatment adherence.[31]

Several studies reporting overall and severe hypoglycemic episodes rates showed no significant change in either outcome with IBGMS use.[15,16,20,23,32] This finding is interesting in itself, given that frequency of SMBG commonly increases with the introduction of IBGMS (see earlier discussion). Because biochemically defined hypoglycemia commonly goes unnoticed by patients,[33,34] it might have been expected that mild hypoglycemia would be detected in IBGMS patients at an increased rate. However, no study has reported such an effect. Rather, studies have reported nonsignificant trends toward a lower hypoglycemia rate or, in 2 cases, a significant decrease in the frequency of moderately severe[17] and severe hypoglycemia.[21] Crucially, this apparent increase in treatment safety with IBGMS was seen in insulin-using[16,17,32,35,36] as well as non–insulin-using patients,[20,21,23] and in studies of patients with poor baseline glycemic control, in which changes in HbA_{1c} level with treatment were particularly striking.

Because use of IBGMS increases monitoring by a health care professional, this intervention is expected to address these psychological barriers to effective pharmacotherapy. In 1 T1D study, patients with IBGMS reported an improved fear of hypoglycemia dimension of the Diabetes-Specific Quality of Life Scale Questionnaire compared with control patients, but this difference did not reach statistical significance ($P = .06$).[17] Given the apparent decline in hypoglycemia incidence in patients using IBGMS, we speculate that broader implementation will help to alleviate fear of hypoglycemia in both health professionals and patients.

IMPROVED GLYCEMIA IN INTERNET BLOOD GLUCOSE MONITORING SYSTEMS: SOME POTENTIAL MECHANISMS

We hypothesized that improved glycemic control seen in IBGMS interventions could arise in part because of increased insulin doses or increased frequency SMBG, which, in some studies of T1D or T2D, correlates with decreased HbA_{1c} level.[37–39]

Improved HbA_{1c} level with IBGMS does not seem to be primarily a consequence of increased insulin doses. As noted earlier,[18,20,22–26] the benefit of IBGMS is not restricted to insulin-using patients. Moreover, among 4 studies reporting insulin dose data, none identified significant differences in insulin dose, comparing baseline and follow-up or between treatment arms.[14–16,36] Thus, it seems that improvement in HbA_{1c} level with IBGMS is largely independent of insulin dose adjustments. This conclusion is consistent with the finding that treatment modification was the least frequent type of feedback for patients to receive by means of IBGMS, with

encouragement being the most frequent type of feedback.[18] Therefore, support and encouragement to increase frequency of SMBG and improve diet and exercise may be more important factors to explain the benefits of IBGMS, compared with any effect on insulin doses.

The beneficial effect of SMBG as an explanation of IBGMS outcomes is more difficult to rule out. SMBG frequency is expected to increase with IBGMS; as noted earlier, several studies have documented this effect.[18,19] However, other studies confirming the efficacy of IBGMS have found no increase in SMBG frequency.[15,16] Moreover, even in studies in which SMBG frequency increased, no correlation has been found between patients' SMBG frequency and improvement in HbA_{1c} level. These studies suggest that although SMBG may contribute to better glycemic control, increased SMBG alone does not explain the glycemic benefits of IBGMS.

In addition to a possible effect of increased SMBG frequency, patients using IBGMS often report increased self-motivation, because of being followed more closely by their health care provider. The number of data uploads from a given patient may offer a quantitative measure of this self-motivation, and this measurement seems to correlate well with IBGMS efficacy. Thus, McMahon and colleagues[23] identified a significant association between data upload frequency and improvement in HbA_{1c} level (decreases of –2.1% and –1.0% in the highest and lowest tertiles, respectively; $P<.02$). Another study, not reaching statistical significance, reported a similar trend.[24]

We propose that glycemic improvements seen in patients on IBGMS result from a combination of factors that stem from increased self-motivation and increased patient-physician communication. Such factors may include improved diet, increased exercise, and, in some cases, increased frequency of SMBG or more effective use of medications.

CARDIOVASCULAR RISK FACTOR CHANGE WITH INTERNET BLOOD GLUCOSE MONITORING SYSTEMS

Decreased risk of cardiovascular (CV) disease is expected in individuals achieving improved HbA_{1c} levels.[3,4] To evaluate whether IBGMS affected patients' CV risk, we examined risk marker changes in various studies of IBGMS. Lipid measures were reported in 12 studies,[14,17–20,23–25,27,28,40] of which 6 showed improvements to at least 1 lipid measure compared with conventional care.[14,18,23,27,28,40] Similarly, of the 7 IBGMS studies reporting blood pressure data,[17,23,25,27,28,40] 4 showed improvements in either systolic or diastolic blood pressure, compared with conventional care.[23,25,27,40] Although these findings are suggestive, longer-term follow-up studies involving more patients may be needed to confirm the CV benefits of IBGMS.[3,4]

QUALITY OF LIFE AND PATIENT SATISFACTION WITH INTERNET BLOOD GLUCOSE MONITORING SYSTEMS

Three studies reported significantly improved quality of life (QOL) in the Internet intervention group, compared with control groups,[17,32,41] and 5 reported no significant difference.[15,21,30]

Of the 3 showing QOL benefits, 1[41] reported a significant improvement in HbA_{1c} levels compared with controls, 1 showed a trend to improvement in HbA_{1c} levels compared with controls,[32] and 1 showed significant improvement in both intervention and control arms, but there was no significance between the groups.[17] This finding suggests that patients may experience benefits from IBGMS beyond those detected by clinical measures. In a study in which HbA_{1c} level change was not significantly different between the IBGMS and control arms, 85% of patients in the intervention

arm believed that the Internet intervention was better than conventional care. Reasons cited included better surveillance of SMBG data by the physician and faster intervention in the case of problems.[35]

COST-EFFECTIVENESS OF INTERNET BLOOD GLUCOSE MONITORING SYSTEMS

No formal pharmacoeconomic studies have been published assessing the cost-effectiveness of IBGMS in widespread implementation. However, some of the randomized controlled studies discussed earlier report comparisons of costs between intervention and control groups.

Cost outcomes have varied substantially over time, with dramatically lower costs seen in recent years, as personal mobile devices became ubiquitous and became a popular platform for Internet medicine. Thus, in the IDEATel study, which started in 2000, health care costs increased 71% to 116% in the intervention group compared with the control group.[42] The costs associated with the intervention arm, more than $8000 per patient per year, were driven mainly by the cost of a specialized home telemedicine unit and associated training and demonstrating costs.[42] However, as early as 2003, Jansa and colleagues[36] reported that, in the absence of technical problems, IBGMS use was associated with a decrease in health care provider costs of €40 (~$55 US) per case over 12 months, because of decreased lengths of appointments in the intervention group.

With more recent Internet-based interventions using patients' Internet-connected personal computers or data-connected cellular phones, Internet intervention costs will likely decrease dramatically. A study that recruited patients who owned iPhones to use the free *Glucose Buddy* app for SMBG tracking estimated an intervention cost of $8.08 AUD (~$7.50 US) per patient over the 6-month study.[30] This modest cost covered the salary of the certified diabetes educator, who spent 5 minutes per patient per week reviewing cases and sending feedback.

From a health care provider's perspective, the automatic uploading of patients' SMBG data increases accuracy of data interpretation by showing the uploaded data in table and graph formats and saves time by automatically incorporating data into electronic medical records. Furthermore, IBGMS Internet or cell phone feedback can potentially replace appointments for dosage adjustments, thus decreasing overall health care costs and freeing up clinic resources.

For patients, IBGMS use has the potential to reduce the number of appointments for dose adjustments or routine follow-up, resulting in decreased travel time. Taking into account travel time and time off work, Biermann and colleagues[35] calculated a savings of €650 (~$900 US) for patients in their intervention, compared with control patients. In this study, physicians followed up with patients by phone every 2 to 4 weeks, compared with monthly in-person visits in the control group. Jansa and colleagues[36] estimated the cost savings of teleconferences instead of in-person visits at €396 (~$548 US) over 12 months. In that study, the intervention group attended 9 teleconferences and 3 hospital appointments versus 12 hospital appointments in the control group.

Long-term cost-benefit analyses, especially in widespread implementations of IBGMS, are needed to show that improved HbA_{1c} level from IBGMS translate to reduced use of health care resources.[43] In principle, such savings could be substantial, because sustained annual cost savings per patient have been reported at $685 to $950 for patients achieving a decrease in HbA_{1c} level of 1% or more.[11] As noted earlier, this level of glycemic improvement is commonly reported in studies of IBGMS.[44]

WIDESPREAD IMPLEMENTATION OF INTERNET BLOOD GLUCOSE MONITORING SYSTEMS

IBGMS is emerging as the standard of care for patients with diabetes in the Canadian province of British Columbia. In this jurisdiction, family physicians, general internists, and endocrinologists are now remunerated for reviewing patient glucose reports. Patients are asked to upload their SMBG data every 2 weeks through a choice of platforms. The patient's physician then reviews the readings and sends feedback via e-mail.

A total of 1200 patients have been enrolled, and outcome data on the first 409 patients showed significant improvement of HbA_{1c} levels after 3 to 9 months of follow-up (**Fig. 2**). Glycemic control improved significantly after introduction of IBGMS in patients with T1D and baseline HbA_{1c} level 6.9% or greater. Similarly, patients with T2D, treated with insulin or oral agents, showed significant improvement in HbA_{1c} level.[44] As was previously reported in a clinical trial, individuals who used the IBGMS frequently (frequent uploaders) experienced greater improvement in glycemic control, relative to infrequent uploaders.[23]

These real-world findings generally agree with results from randomized controlled trials, in that IBGMS seems effective in T2D, irrespective of baseline glycemia or mode of treatment, as well as in T1D for patients with poor glycemic control. Moreover, more frequent use of the system to upload of SMBG data (presumably reflecting greater patient self-motivation) was associated with improved HbA_{1c} levels.

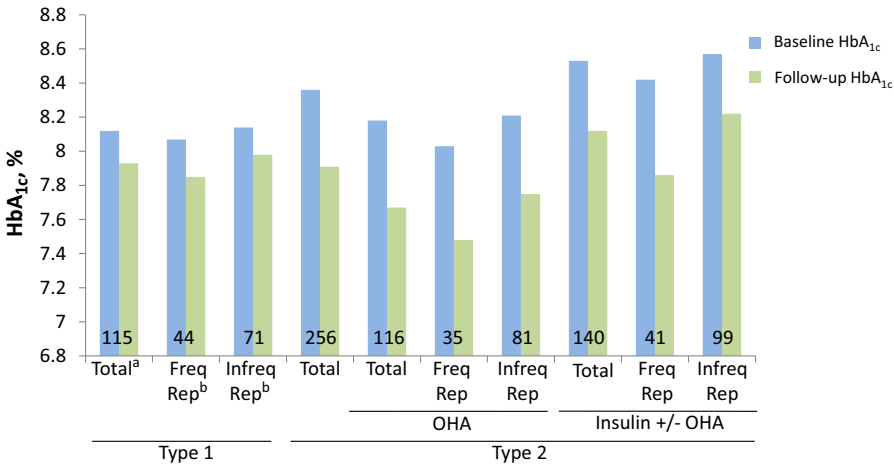

Fig. 2. Mean HbA_{1c} level at baseline and follow-up in patients with IBGMS who upload their blood glucose data frequently (Freq Rep) versus infrequently (Infreq Rep). When patients with HbA_{1c} level less than 6.9% were excluded, patients with T1D showed a significant improvement in HbA_{1c} level at follow-up (P<.01). Total T2D, T2D on OHA only, and T2D patients on insulin ± OHA all showed significant decreases in HbA_{1c} level at follow-up (all P<.001). P = .05 for frequent reporters compared with infrequent reporters for each type of diabetes. [a] Excluding patient HbA_{1c} level less than 6.9%; [b] excluding patient HbA_{1c} level less than 7.4%. OHA, oral hypoglycemic agent. (*Data from* Tildesley HD, Conway ME, Ross SA, et al. Review of the effect of internet therapeutic intervention in patients with type 1 and type 2 diabetes. Diabetes Care 2014;37(2):e31–2.)

Box 1
Sample messages to patients

High in the AM; please increase evening metformin to 750 mg at supper. Let's see if there is any shift in 2 weeks.

Your lunch value is excellent, but supper is showing variability. Please work on having supper at the same time each day, which should improve consistency, and report again in 2 weeks. Thanks.

Your sugar levels are a little high at lunch and supper. Try a carb ratio of 10:1 at breakfast and lunch. Please report again in 2 weeks. Thanks

PRACTICAL TIPS FOR EFFECTIVE INTERNET BLOOD GLUCOSE MONITORING SYSTEMS

One key to efficient implementation of IBGMS is the use of clear and standardized reports of patient glucose levels. Reports should clearly indicate time of day, average glucose levels, range and standard deviation (SD) of glucose values. They should be organized so that raw data, as well as summary data, can be accessed easily. As a general rule, testing frequency should be such that there are at least 10 values for a given time of day across the reporting period, for instance 10 before breakfast measurements within 2 weeks, or else the statistics may be less accurate to their true values. Most glucose meters and some insulin pumps and sensors are designed to facilitate the uploading and transmission of stored data.

One rule of thumb is to first check the SD of glucose levels by time of day. In general, if the SD is less than 50 mg/dL (<2.8 mmol/L for measurements in SI units), the data can be used for determining appropriate therapeutic changes. If the SD is increased, therapeutic changes should be delayed until the patient is able to provide more consistent values. Larger SD values are related to meal timing, meal content, timing of medications, or possibly, major stresses, which result in less focus on diabetes self-management. Possible causes could include major life events such as the death of a family member, recent unemployment, or development of a mental health disorder; for such situations, the cause of stress should be addressed directly, often with the aid of a mental health professional. The next step is to decide if average values are at target by time of day; if not, medications are adjusted according to their onset and duration of action and effect.

With practice, reports can be reviewed efficiently, allowing a health professional to offer clear guidance in a concise text or e-mail message to the patient. Typically, such a message suggests changes in diet (eg, carbohydrate ratio for specific meals) or in the timing or dose of insulin or an oral agent. The patient should always be asked to follow up at a specified time (eg, 2 weeks later) to discuss the outcomes of these changes (**Box 1**).

SUMMARY AND FUTURE PERSPECTIVES

Telehealth (Internet-based and telephone-based) interventions have been increasingly discussed in recent clinical practice guidelines. The CDA 2013 Clinical Practice Guidelines recommend that technologically based home blood glucose monitoring systems be integrated into self-management education interventions, to improve glycemic control.[6] Likewise, the ADA 2013 Standards of Medical Care Position Statement indicates that telehealth can help provide self-management education and support.[10]

We have argued here that IBGMS is broadly useful in patients with T1D and T2D, in large part because it improves communication between patients and their health care providers. Widespread rollout of IBGMS is ongoing in some locations, and experience from these nascent programs should answer lingering questions about the benefits and cost-effectiveness of the approach. The findings are encouraging. Since 2011, the Canadian province of British Columbia has reimbursed endocrinologists for the review of IBGMS data.

Although a cost analysis of this IBGMS implementation is not available, a health professional is typically able to review patient data and send feedback to the patient via e-mail in just a few minutes per case, performed every 2 to 4 weeks. Most recently, the United Kingdom has undertaken a 30-month study called *HeLP-Diabetes* (Healthy Living for People with type 2 Diabetes). The study will be conducted in 2 inner city London boroughs, in which there are ~14,000 potential users of *HeLP-Diabetes*,[45] making this the largest IBGMS program yet designed. Data from this study are eagerly awaited.

Available study data on IBGMS support the clinical usefulness of this approach to diabetes management, with improved glycemic control in all types of diabetes patients and no increase in hypoglycemia risk. IBGMS seems to be well accepted by patients and to involve minimal time commitment from the health professional, with some evidence of health care cost savings and reduced burden on clinical resources. IBGMS thus warrants consideration, both for widespread implementation and for insurance coverage.

ACKNOWLEDGMENTS

The authors wish to thank John Ashkenas, PhD (SCRIPT, Toronto, Canada) for editorial assistance. H.D. Tildesley gratefully acknowledges the Endocrine Research Society for financial support for this project.

REFERENCES

1. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. The Diabetes Control and Complications Trial Research Group. N Engl J Med 1993;329(14):977–86.
2. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). UK Prospective Diabetes Study (UKPDS) Group. Lancet 1998;352(9131):837–53.
3. Holman RR, Paul SK, Bethel MA, et al. 10-year follow-up of intensive glucose control in type 2 diabetes. N Engl J Med 2008;359(15):1577–89.
4. Nathan DM, Cleary PA, Backlund JY, et al. Intensive diabetes treatment and cardiovascular disease in patients with type 1 diabetes. N Engl J Med 2005;353(25):2643–53.
5. Nathan DM, DCCT/EDIC Research Group. The diabetes control and complications trial/epidemiology of diabetes interventions and complications study at 30 years: overview. Diabetes Care 2014;37(1):9–16.
6. Cheng AY, Lau DC. The Canadian Diabetes Association 2013 clinical practice guidelines–raising the bar and setting higher standards! Can J Diabetes 2013;37(3):137–8.
7. Braga M, Casanova A, Teoh H, et al. Treatment gaps in the management of cardiovascular risk factors in patients with type 2 diabetes in Canada. Can J Cardiol 2010;26(6):297–302.

8. Hoerger TJ, Segel JE, Gregg EW, et al. Is glycemic control improving in US adults? Diabetes Care 2008;31(1):81–6.
9. Ali MK, Bullard KM, Saaddine JB, et al. Achievement of goals in US diabetes care, 1999-2010. N Engl J Med 2013;368(17):1613–24.
10. American Diabetes Association. Standards of medical care in diabetes–2014. Diabetes Care 2014;37(Suppl 1):S14–80.
11. Malanda UL, Welschen LM, Riphagen II, et al. Self-monitoring of blood glucose in patients with type 2 diabetes mellitus who are not using insulin. Cochrane Database Syst Rev 2012;(1):CD005060.
12. Ross SA, Tildesley HD, Ashkenas J. Barriers to effective insulin treatment: the persistence of poor glycemic control in type 2 diabetes. Curr Med Res Opin 2011;27(Suppl 3):13–20.
13. Tildesley HD, Mazanderani AB, Chan JH, et al. Efficacy of A1c reduction using internet intervention in patients with type 2 diabetes treated with insulin. Can J Diabetes 2011;35(3):250–3.
14. Tildesley HD, Mazanderani AB, Ross SA. Effect of Internet therapeutic intervention on A1C levels in patients with type 2 diabetes treated with insulin. Diabetes Care 2010;33(8):1738–40.
15. Charpentier G, Benhamou PY, Dardari D, et al. The Diabeo software enabling individualized insulin dose adjustments combined with telemedicine support improves HbA1c in poorly controlled type 1 diabetic patients: a 6-month, randomized, open-label, parallel-group, multicenter trial (TeleDiab 1 Study). Diabetes Care 2011;34(3):533–9.
16. Montori VM, Helgemoe PK, Guyatt GH, et al. Telecare for patients with type 1 diabetes and inadequate glycemic control: a randomized controlled trial and meta-analysis. Diabetes Care 2004;27(5):1088–94.
17. Rossi MC, Nicolucci A, Lucisano G, et al. Impact of the "diabetes interactive diary" telemedicine system on metabolic control, risk of hypoglycemia, and quality of life: a randomized clinical trial in type 1 diabetes. Diabetes Technol Ther 2013;15(8):670–9.
18. Cho JH, Chang SA, Kwon HS, et al. Long-term effect of the Internet-based glucose monitoring system on HbA1c reduction and glucose stability: a 30-month follow-up study for diabetes management with a ubiquitous medical care system. Diabetes Care 2006;29(12):2625–31.
19. Kwon HS, Cho JH, Kim HS, et al. Establishment of blood glucose monitoring system using the internet. Diabetes Care 2004;27(2):478–83.
20. Kim C, Kim H, Nam J, et al. Internet diabetic patient management using a short messaging service automatically produced by a knowledge matrix system. Diabetes Care 2007;30(11):2857–8.
21. Bujnowska-Fedak MM, Puchala E, Steciwko A. The impact of telehome care on health status and quality of life among patients with diabetes in a primary care setting in Poland. Telemed J E Health 2011;17(3):153–63.
22. Kim SI, Kim HS. Effectiveness of mobile and internet intervention in patients with obese type 2 diabetes. Int J Med Inform 2008;77(6):399–404.
23. McMahon GT, Gomes HE, Hickson Hohne S, et al. Web-based care management in patients with poorly controlled diabetes. Diabetes Care 2005;28(7):1624–9.
24. Ralston JD, Hirsch IB, Hoath J, et al. Web-based collaborative care for type 2 diabetes: a pilot randomized trial. Diabetes Care 2009;32(2):234–9.
25. Shea S, Weinstock RS, Teresi JA, et al. A randomized trial comparing telemedicine case management with usual care in older, ethnically diverse, medically

underserved patients with diabetes mellitus: 5 year results of the IDEATel study. J Am Med Inform Assoc 2009;16(4):446–56.
26. Yoon KH, Kim HS. A short message service by cellular phone in type 2 diabetic patients for 12 months. Diabetes Res Clin Pract 2008;79(2):256–61.
27. Bond GE, Burr R, Wolf FM, et al. The effects of a web-based intervention on the physical outcomes associated with diabetes among adults age 60 and older: a randomized trial. Diabetes Technol Ther 2007;9(1):52–9.
28. Stone RA, Rao RH, Sevick MA, et al. Active care management supported by home telemonitoring in veterans with type 2 diabetes: the DiaTel randomized controlled trial. Diabetes Care 2010;33(3):478–84.
29. Tjam EY, Sherifali D, Steinacher N, et al. Physiological outcomes of an internet disease management program vs. in-person counselling: a randomized, controlled trial. Can J Diabetes 2006;30(4):397–405.
30. Kirwan M, Vandelanotte C, Fenning A, et al. Diabetes self-management smartphone application for adults with type 1 diabetes: randomized controlled trial. J Med Internet Res 2013;15(11):e235.
31. Cryer PE. Hypoglycaemia: the limiting factor in the glycaemic management of type I and type II diabetes. Diabetologia 2002;45(7):937–48.
32. Benhamou PY, Melki V, Boizel R, et al. One-year efficacy and safety of Web-based follow-up using cellular phone in type 1 diabetic patients under insulin pump therapy: the PumpNet study. Diabetes Metab 2007;33(3):220–6.
33. Chico A, Vidal-Rios P, Subira M, et al. The continuous glucose monitoring system is useful for detecting unrecognized hypoglycemias in patients with type 1 and type 2 diabetes but is not better than frequent capillary glucose measurements for improving metabolic control. Diabetes Care 2003;26(4):1153–7.
34. Weber KK, Lohmann T, Busch K, et al. High frequency of unrecognized hypoglycaemias in patients with type 2 diabetes is discovered by continuous glucose monitoring. Exp Clin Endocrinol Diabetes 2007;115(8):491–4.
35. Biermann E, Dietrich W, Rihl J, et al. Are there time and cost savings by using telemanagement for patients on intensified insulin therapy? A randomised, controlled trial. Comput Methods Programs Biomed 2002;69(2):137–46.
36. Jansa M, Vidal M, Viaplana J, et al. Telecare in a structured therapeutic education programme addressed to patients with type 1 diabetes and poor metabolic control. Diabetes Res Clin Pract 2006;74(1):26–32.
37. Hirsch IB, Bode BW, Childs BP, et al. Self-monitoring of blood glucose (SMBG) in insulin- and non-insulin-using adults with diabetes: consensus recommendations for improving SMBG accuracy, utilization, and research. Diabetes Technol Ther 2008;10:419–39.
38. Karter AJ, Parker MM, Moffet HH, et al. Longitudinal study of new and prevalent use of self-monitoring of blood glucose. Diabetes Care 2006;29(8):1757–63.
39. Strowig SM, Raskin P. Improved glycemic control in intensively treated type 1 diabetic patients using blood glucose meters with storage capability and computer-assisted analyses. Diabetes Care 1998;21(10):1694–8.
40. Harno K, Kauppinen-Makelin R, Syrjalainen J. Managing diabetes care using an integrated regional e-health approach. J Telemed Telecare 2006;12(Suppl 1):13–5.
41. Bond GE, Burr RL, Wolf FM, et al. The effects of a web-based intervention on psychosocial well-being among adults aged 60 and older with diabetes: a randomized trial. Diabetes Educ 2010;36(3):446–56.
42. Moreno L, Dale SB, Chen AY, et al. Costs to medicare of the informatics for diabetes education and telemedicine (IDEATel) home telemedicine demonstration: findings from an independent evaluation. Diabetes Care 2009;32(7):1202–4.

43. Malanda UL, Bot SD, Nijpels G. Self-monitoring of blood glucose in noninsulin-using type 2 diabetic patients: it is time to face the evidence. Diabetes Care 2013;36(1):176–8.
44. Tildesley HD, Conway ME, Ross SA, et al. Review of the effect of internet therapeutic intervention in patients with type 1 and type 2 diabetes. Diabetes Care 2014;37(2):e31–2.
45. Ross J, Stevenson F, Dack C, et al. Evaluating the implementation of HeLP-Diabetes within NHS services: study protocol. BMC Health Serv Res 2014;14:51.
46. Trief PM, Teresi JA, Izquierdo R, et al. Psychosocial outcomes of telemedicine case management for elderly patients with diabetes: the randomized IDEATel trial. Diabetes Care 2007;30(5):1266–8.
47. Gomez EJ, Hernando ME, Garcia A, et al. Telemedicine as a tool for intensive management of diabetes: the DIABTel experience. Comput Methods Programs Biomed 2002;69(2):163–77.
48. McCarrier KP, Ralston JD, Hirsch IB, et al. Web-Based Collaborative Care for Type 1 Diabetes: A Pilot Randomized Trial. Diabetes Technol Ther 2009;11(4):211–7.