Background: Instruments for self-monitoring of glucose (SMBG) are increasingly used by diabetic patients. Information is limited on how patients use and interpret SMBG results, and no quality specifications for such instruments are based on the opinions of patients.

Methods: Type 1 diabetic patients (n = 201) filled in a questionnaire eliciting daily limits for blood glucose (BG) and changes of BG considered significant at different glucose concentrations. From these responses, patient-derived quality specifications were calculated in different clinical situations with low, intermediate, and high BG concentrations.

Results: Mean age of the patients was 31.8 years, mean diabetes duration was 14.7 years, and mean SMBG duration was 10.0 years with a mean frequency of 11.2 measurements/week. The threshold for hypoglycemic symptoms was 3.0 mmol/L (54 mg/dL), and the mean daily BG target window was 4.3–10.4 mmol/L (77–187 mg/dL). The mean absolute BG changes producing actions from the patients ranged from 1.1 mmol/L (20 mg/dL) to 3.6 mmol/L (65 mg/dL). The analytical quality specifications for imprecision depended on the clinical situation. Excluding the hypoglycemic situation, the analytical CV needed to fulfill the expectations of 75% of the patients was 6.4–9.7%. The analytical quality specification for CV at hypoglycemic concentrations was 3.1%.

Conclusions: Instruments for self-measurements of glucose with an imprecision (CV) of ≤5% and bias ≤5% meet the expectations of >75% of patients in clinical situations other than hypoglycemia.

© 2001 American Association for Clinical Chemistry
Materials and Methods

Only individuals with type 1 diabetes mellitus were included in the study during the recruitment period from March to November 1998. Patients were included consecutively at their scheduled follow-up visits with a diabetes specialist or a diabetes nurse at the diabetes outpatient clinic, Rogaland Central Hospital (Stavanger, Norway).

The study was based on self-reported data obtained with a questionnaire. The questionnaire was developed and evaluated in cooperation with a diabetes specialist, diabetes nurses, and patients. It was piloted, tested, and evaluated with the help of 10 patients before study recruitment was initiated. Care was taken to seek information on what patients in reality mean and do, and not what they think should be done. For this reason the questionnaire was handed out by assistant personnel to patients arriving the clinic. It was always filled in before the nurse/doctor consultation and without any primary assistance or professional influence. Patients anonymously delivered their responses in sealed envelopes.

![Fig. 1. Questionnaire assessing SMBG.](image-url)
Except for baseline characteristics, the questionnaire (translated into English) is reproduced in Fig. 1. Questions focused on BG thresholds for action, changes to be followed by actions, and the measured differences needed for patients to be sure that the BG had actually changed. In questions 6 and 8, patients were specifically asked to use the BG concentrations stated by themselves in question 4. Some patients still misunderstood how to do this and responded in a way that produced negative values, which consequently were excluded from the data analysis.

The critical difference (CD) is defined as the difference needed between two consecutive test results to be certain, with a given probability, that the two results truly are different (i.e., that the change is not caused solely by analytical and biological variation). The formula used is (10, 11):

$$CD = \text{bias} + z\text{-value} \times \sqrt{\frac{2}{\text{CV}_a^2 + \text{CV}_i^2}}$$

$$= \text{bias} + 2.3 \times \sqrt{\frac{2}{\text{CV}_a^2 + \text{CV}_i^2}}$$

CV$_a$ is the analytical CV, and CV$_i$ is the mean within-subject (intraindividual) CV for BG. A CV$_i$ of 5% (12, 13) was used in all of the clinical situations addressed in the questionnaire, although it could be argued that it could have been omitted in some of the situations where two measurements were taken 1 h apart. Not using CV$_i$ in the calculations for these situations would not, however, have influenced the conclusions of the study. The within-subject variation of 5% refers to healthy individuals, and it is probably higher in patients with diabetes. To our knowledge, no studies have examined this. Higher within-subject variation would have produced lower CV$_a$ values (see below). We assessed unidirectional changes, and the $z$-value for one-sided tests and 95% probability were used. CV$_a$ was calculated using the formula above with patient responses used as CDs. Thus by rearranging the formula:

$$\text{CV}_a = \sqrt{(\text{CD} - \text{bias})^2 / 2z^2} - \text{CV}_i^2$$

The bias component of the CD was either set to be a certain percentage of the BG result or was included in CV$_a$, which then would comprise long-term variations such as batch-to-batch variation. Thus, using the data on CDs in BG, we could set specific quality goals for the instruments as needed by the patients.

Continuous variables were compared using the Student $t$-test or nonparametric tests when appropriate. We used the Pearson correlation coefficient. The level of statistical significance was set to 5%.

**Results**

Type 1 diabetic patients (n = 201) were enrolled in the study. Only a few patients unable to perform SMBG
themselves were not included, and no patients refused to participate. The patients had performed SMBG for a mean of 10.0 years. The participating women were older and had longer duration of diabetes than did the men. Base-
line age, diabetes characteristics, and SMBG frequency for all patients stratified by sex are given in Table 1. Six
patients performed SMBG less than once per week, and seven patients were diagnosed with diabetes and had initiated SMBG within the last year. Females performed SMBG more frequently (12.8/week vs 9.5/week; \( P = 0.02 \)) than males. SMBG frequency was not significantly corre-
lated to number of years with diabetes (\( r = 0.05; P = 0.5 \)).

Except for data presented in Table 1, there were no difference in responses between women and men. Results on BG thresholds and SMBG targets for men and women are therefore combined and are presented in Table 2. The mean hypoglycemia threshold was 3 mmol/L (54 mg/dL). The daily BG target window, within which the diabetic patients wanted their BG concentrations to re-
main, was calculated by simply subtracting “daily lower BG target limit” from “daily upper BG target limit”. The
mean daily BG target window was 6.0 ± 2.7 mmol/L (108 ± 49 mg/dL). More than 95% of the participants responded adequately to the questions in this part of the questionnaire. Only a few patients had problems giving exact BG concentrations on items such as hypoglycemic thresholds and threatening high BG. Individuals report-
ing low hypoglycemic thresholds also reported a low daily target limit (\( r = 0.25 \)), whereas those reporting high
hyperglycemic thresholds frequently reported high daily upper limits (\( r = 0.37 \)) and large BG target windows (\( r = 0.28 \)). These correlations were all significant at \( P < 0.01 \). No significant correlations were found between items assessing low and high BG concentrations. Responses on BG targets and thresholds did not show significant asso-
ciations with any of the baseline characteristics presented.

The final part of the questionnaire dealt with patients’ considerations and interpretations of measured BG con-
centrations in different situations representing intermedi-
ate, high, and low BG concentrations. These questions were more difficult for some of the patients to understand and yielded overall response rates (including missing and inadequate responses) for individual questions ranging from 66% to 90%, with response rates <80% for questions

---

**Table 3. BG differences deemed necessary to take actions or stated to represent a true change, and resulting quality specifications for imprecision.**

<table>
<thead>
<tr>
<th>Question</th>
<th>BG change, mmol/L</th>
<th>Change, %</th>
<th>Calculated CVa%</th>
</tr>
</thead>
<tbody>
<tr>
<td>5A: BG increasing from 8.0 mmol/L</td>
<td>3.4 ± 2.2</td>
<td>25.0</td>
<td>9.7</td>
</tr>
<tr>
<td>25th percentile</td>
<td>2.0</td>
<td>25.0</td>
<td>9.7</td>
</tr>
<tr>
<td>50th percentile</td>
<td>2.4</td>
<td>30</td>
<td>12</td>
</tr>
<tr>
<td>75th percentile</td>
<td>7.0</td>
<td>50.0</td>
<td>21</td>
</tr>
<tr>
<td>5B: BG decreasing from 8.0 mmol/L</td>
<td>3.1 ± 1.3</td>
<td>25.0</td>
<td>9.7</td>
</tr>
<tr>
<td>25th percentile</td>
<td>2.0</td>
<td>25.0</td>
<td>9.7</td>
</tr>
<tr>
<td>50th percentile</td>
<td>3.0</td>
<td>37.5</td>
<td>16</td>
</tr>
<tr>
<td>75th percentile</td>
<td>4.0</td>
<td>50.0</td>
<td>21</td>
</tr>
<tr>
<td>6: BG increasing from daily upper target limit</td>
<td>3.4 ± 2.2</td>
<td>20.0</td>
<td>7.1</td>
</tr>
<tr>
<td>25th percentile</td>
<td>2.0</td>
<td>20.0</td>
<td>7.1</td>
</tr>
<tr>
<td>50th percentile</td>
<td>3.0</td>
<td>28.6</td>
<td>11</td>
</tr>
<tr>
<td>75th percentile</td>
<td>4.0</td>
<td>50.0</td>
<td>21</td>
</tr>
<tr>
<td>7: BG decrease 1 h after hyperglycemia action</td>
<td>3.6 ± 1.9</td>
<td>18.6</td>
<td>6.4</td>
</tr>
<tr>
<td>25th percentile</td>
<td>2.0</td>
<td>18.6</td>
<td>6.4</td>
</tr>
<tr>
<td>50th percentile</td>
<td>3.0</td>
<td>26.4</td>
<td>10</td>
</tr>
<tr>
<td>75th percentile</td>
<td>4.0</td>
<td>35</td>
<td>14</td>
</tr>
<tr>
<td>8: BG decreasing from daily lower target limit</td>
<td>1.1 ± 0.8</td>
<td>13.6</td>
<td>3.1</td>
</tr>
<tr>
<td>25th percentile</td>
<td>0.5</td>
<td>13.6</td>
<td>3.1</td>
</tr>
<tr>
<td>50th percentile</td>
<td>1.0</td>
<td>25</td>
<td>9.7</td>
</tr>
<tr>
<td>7th percentile</td>
<td>1.5</td>
<td>30.0</td>
<td>12</td>
</tr>
<tr>
<td>9: BG increase 1 h after hypoglycemia action</td>
<td>2.6 ± 1.5</td>
<td>42.9</td>
<td>18</td>
</tr>
<tr>
<td>25th percentile</td>
<td>1.6</td>
<td>42.9</td>
<td>18</td>
</tr>
<tr>
<td>50th percentile</td>
<td>2.5</td>
<td>66.7</td>
<td>29</td>
</tr>
<tr>
<td>75th percentile</td>
<td>3.0</td>
<td>100.0</td>
<td>43</td>
</tr>
</tbody>
</table>

\( CVa = \sqrt{(CV_{i}^{2} + CD^{2} \over 2}) - CV_{i}^{2}. \)

Numbers refer to questions in Fig. 1.

---

![Fig. 2. Relationship between allowable imprecision and bias when the CD is 22% (reflecting optimum quality) or 30% (reflecting desirable quality). See text for details.](image-url)
6 and 8. The nonresponders were not different from the responders with respect to baseline characteristics or hypo- and hyperglycemic thresholds.

The mean absolute BG changes taken to represent a true change or producing actions ranged from 1.1 mmol/L (20 mg/dL) to 3.6 mmol/L (65 mg/dL), depending on the clinical situation described for the patient. The results and variability of BG changes stated are shown for the 25th, 50th, and 75th percentiles in Table 3. Table 3 also shows the quality specifications for SMBG (calculated CVa) derived from the patients’ responses in the different clinical situations (not including a specified bias component). CVa is given as the lower 25th percentile (optimum quality), 50th percentile (desirable quality), and 75th percentile (minimum quality) (9). The variation in responses was substantial and was not associated with baseline characteristics. Optimum and desirable quality specifications were rather similar for the four first situations (questions 5–7) with CVas of 6.4–9.7% and 10–16%, respectively.

If the CD also included a bias component, e.g., change of batch or instrument, the allowable CVa decreased. The relationship between CVa and the bias component is shown in Fig. 2 for CDs reflecting optimum and desirable quality specifications. The values in Fig. 2 reflect the mean CDs of the four first clinical situations (Table 3). The hypoglycemic situation (clinical situations 8 and 9 in Fig. 1) was different, and the patients here concluded with a lower CVa for decreasing glucose concentrations (question 8) and a higher CVa to estimate whether glucose had indeed increased (question 9) after actions to alleviate hypoglycemia. For the responders, a high CVa response on one question correlated positively and significantly with a high CVa on the other questions (P < 0.05).

**Discussion**

SMBG as a cornerstone in diabetes treatment is unquestionable today. It is reasonable that frequent and correct SMBG will be of great benefit to all patients trying to improve their metabolic control. The patients included in our study were people with longstanding diabetes, were experienced in judging their daily BG concentrations and acting or not acting on them, and used various BG instruments, finding the critical balance between metabolic control and acceptable quality of life.

Symptoms of hypoglycemia often change or become weaker in patients who have had diabetes for many years, thereby increasing the individual’s need for SMBG. In addition, the finding of a mean frequency of SMBG of 11 times per week indicates that it is possible to use SMBG as a tool to improve metabolic control. Referring to the Diabetes Control and Complications Trial, ADA has stated that type 1 patients should measure BG three or four times per day to facilitate tight metabolic control (3, 6, 14). This would mean 21–28 measurements per week, which is considerably more frequent than our type 1 diabetic patients reported. We are not confident that the ADA-recommended SMBG frequency would be either achievable or right in our regular diabetes follow-up clinic. Many barriers, both “practical” and “emotional”, limit performing SMBG regularly (15, 16). In fact, the resulting metabolic control rests on the actions taken based on SMBG, and the current literature gives only weak support to the direct association between performance and frequency of SMBG and metabolic control (17–19).

The responders’ mean threshold for hypoglycemic symptoms of 3 mmol/L (54 mg/dL) compares well with the literature (20–22). The variability of the concentrations in the responses might indicate some degree of unawareness of hypoglycemia or possibly that the instruments used have a variable bias in this lower range. Patients’ demands on their instruments were greatest in the situation described in question 8 with decreasing BG below the lower daily target limit, showing that a calculated CVa of 3.1% was needed to satisfy 75% of the patients (optimum quality). Compared with the other clinical situations, this is very low. It may, however, also reflect that this change is very important for the patients to detect. Therefore, in this specific situation, they probably react on a change with <95% probability that this change is really true. Patients find it highly important to detect BG below the lower daily target limit and therefore accept a higher number of “false reactions”. With the probability set to 80%, the optimum and desirable analytical imprecision (CVa) will increase to 13% and 20%, respectively. In a similar way, diabetic patients probably want to be close to 100% certain that BG has increased in clinical situations where actions are taken to alleviate hypoglycemia (question 9). When the 95% probability was replaced with 99.5% probability in question 9, the resulting optimum and desirable quality specification (CVa) decreased to 11% and 18%, respectively.

A daily BG target window of 4.3–10.4 mmol/L (77–187 mg/dL, mean values) is in line with current treatment recommendations (3). However, this means that meters used in reality must provide the analytical quality needed to maintain BG concentrations within a 6 mmol/L range. The BG CDs in this range given by the patients in questions 5A and 5B were ~2.0 mmol/L (36 mg/dL) and 2.4–3.0 mmol/L (46–54 mg/dL), representing optimum and desirable total error, respectively. For diabetic patients to be 95% certain that the BG value is within the target window, the result should be between 6.3 (i.e., 4.3 + 2.0) mmol/L (113 mg/dL) and 8.4 (i.e., 10.4 – 2.0) mmol/L (151 mg/dL) when BG is measured with optimum quality (i.e., a total error <2 mmol/L). Desirable analytical quality would make it difficult, and minimum analytical quality would make it impossible, for patients to verify that their BG concentrations truly were within this window. These calculations presuppose that the bias component is zero or is included in CVa. Excluding the hypoglycemia situation, the analytical quality specifications (CVa) for optimum quality (25th percentile) ranged...
from 6.4% to 9.7%, and for desirable quality (50th percentile), they ranged from 10% to 16%, depending on the clinical situation.

In many clinical situations, it will be relevant to include a specified bias component in the calculations because many patients use different batch numbers at the same time or use different instruments and batches, depending on where the measurement is performed (e.g., one instrument at work and another at home). The mean CDs for the clinical situations, excluding the hypoglycemic situation, were 22% and 30% for optimum and desirable quality, respectively. On the basis of these numbers and setting the imprecision to 5%, bias components of 5% (optimum quality) and 13% (desirable quality), respectively, could be allowed (Fig. 2).

The ADA has stated that SMBG systems should be able to achieve a total (analytical + user) error of 10% at glucose concentrations of 1.67–22.2 mmol/L (30–400 mg/dL) and that future systems should be manufactured with 5% analytical error as a goal (23). From our data, we see that patients expect the highest analytical quality from their instruments when BG decreases below their daily lower limit and expect less in hyperglycemic ranges. Such an interpretation implies that meter quality specifications should be different in the high and low BG ranges. This aspect has not been dealt with in the literature (24, 25).

In a study similar to ours, Weiss et al. (26) also found that quality demands for BG set by patients were highest at the “lower acceptable limit”. Their study was also based on data from a questionnaire, but it included only 30 type 1 and 20 type 2 patients, and the authors personally interviewed all patients, with possible influence on their responses. In addition, the patients were probably highly skilled and motivated because some of them were participating in the Diabetes Control and Complications Trial at the time (6, 26). Our study was performed 5 years later, with better SMBG instruments available, but patients’ expectations regarding analytical quality were quite similar except for the situation of hypoglycemia. On the basis of patients’ responses, Weiss et al. (26) recommended an imprecision of ≤7%. The maximum allowable change was used to calculate CV, assuming differences strictly attributable to analytical imprecision and ignoring biological variation (27). Including within-subject variation in the calculations naturally leads to stricter estimates of analytical quality, and consequently the 7% recommended by Weiss et al. (26) would be reduced to 5%. In the same study (26), physicians’ expectations were different from patients’, with a CV of 14% at the lower acceptable limit (13% when within-subject variation was taken into account) and 7% (5%) at the limit of hyperglycemia. This probably reflects that patients have their main focus on hypoglycemia, whereas physicians tend to focus on metabolic control. Thus, it seems that the quality specifications should be rather similar in both the high and low ranges of glucose measurements, taking the opinions of both patients and physicians into account.

Applying a quality specification for imprecision with a CV equal to 5% and a bias of 5% to our study population would be satisfactory for close to or more than 75% of the patients in all clinical situations except for hypoglycemia.

The International Organization for Standardization has suggested a performance goal for BG-measuring systems under ideal conditions, requiring that 95% of the individual test results should be within ± 20% of a comparative method and within ± 1.1 mmol/L (20 mg/dL) for BG concentrations <5.5 mmol/L (99 mg/dL) (28). This would produce a CV of ~10% with 0% bias and a CV of 5% with a bias of 12% corresponding to desirable performance as judged by the diabetic patients in the present study. The quality specifications set by the International Organization for Standardization should apply to the quality of the instruments in the hands of the diabetic patients. Quality specifications under ideal conditions should be stricter.

When establishing criteria for BG meters, the persons establishing the criteria should recognize patient beliefs and perform quality control on new BG monitors in the hands of the users and not in tailored research settings. It is not to be expected that most patients have detailed knowledge about analytical imprecision, bias, and other types of error. Thus the patient-derived analytical quality specifications depend on how the patients actually interpret the results from the instruments, and the specifications will change when the patients’ interpretation of the results change, e.g., by better education. On the basis of our data, we recommend a CV of 5% for BG monitors; in addition, the bias should be as small as possible and at least ≤5%. We believe that it will be unrealistic to set goals based on the hypoglycemic situation only, and we recommend that patients be better educated about BG measurements and interpretation of results in general.

In conclusion, we have found that persons with type 1 diabetes perform SMBG frequently, and the possibility to improve metabolic control based on self-measurements exists. Most patients have clear views on target concentrations and BG thresholds based on SMBG. Patients expect meters to provide high analytical quality over the entire range of BG measurements; these expectations are difficult to meet with current BG monitors. Quality specifications for BG monitors set by the patients should be challenged with studies testing current BG meters in the hands of the users. In line with the ADA recommendations for the future, we also recommend that current meters should have an imprecision of 5% or less to meet patient expectations. Education in SMBG should focus on the limitations of portable BG meters and errors involved in the interpretation of BG results. However, education should also focus on therapeutic actions to be taken in a variety of clinical situations, and not only when the measured BG is in the low range.
References


