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# Performance of Afinion $HbA_{1c}$ measurements in general practice as judged by external quality assurance data

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**Abstract**

**Background:** It has been debated whether point-of care (POC) glycated hemoglobin ($HbA_{1c}$) measurements methods can be used for diagnosing persons with diabetes mellitus. The aim of this study was to evaluate the analytical performance of the POC Afinion $HbA_{1c}$ system in the hands of the users, and to investigate which predictors that were associated with good participant performance.
**Methods:** External quality assurance (EQA) data from seven surveys in 2017–2018 with a total of 5809 Afinion participants from a POC total quality system in Norway were included in this study (response rate 90%). The control materials were freshly drawn pooled EDTA whole blood. Each participant was evaluated against the analytical performance specification of ±6% from the target value, while the Afinion system was evaluated against the pooled within-laboratory CV <2%, the between-laboratory CV <3.5%, and bias <0.3%$HbA_{1c}$. Logistic regression analyses were used to investigate which factors were associated with good participant performance.
**Results:** The participant pass rates for each survey varied from 98.2% to 99.7%. The pooled within-laboratory CV varied from 1.3% to 1.5%, the between-laboratory CV varied from 1.5% to 2.1%, and bias varied between −0.17 and −0.01 %$HbA_{1c}$ in all surveys. Reagent lot was the only independent factor to predict good participant performance.
**Conclusions:** Afinion $HbA_{1c}$ fulfilled the analytical performance specifications and is robust in the hands of the users. It can therefore be used both in diagnosing and monitoring persons with diabetes mellitus, given that the instrument is monitored by an EQA system.

**Keywords:** analytical performance specifications; diabetes mellitus; external quality assurance; glycated hemoglobin; point-of-care testing.

## Introduction

The level of glycated hemoglobin ($HbA_{1c}$) plays a critical role in diagnosing and monitoring diabetes mellitus. Acceptable precision and trueness of the $HbA_{1c}$ measurement methods are therefore essential. Point-of-care testing (POCT) is widely used for $HbA_{1c}$ monitoring. It reduces the turnaround times and may increase the efficacy of the service provided to patients [1, 2]. When used both for diagnostic and monitoring purposes, the POCT $HbA_{1c}$ measurement methods should meet the same analytical performance specifications as central laboratories.

External quality assurance (EQA) is a tool for the individual laboratories to assess their own performance, compare results with others or, if a commutable material is used, compare results with a target value set by a reference measurement procedure. For POCT measurement methods, it is important to evaluate performance in the hands of the intended users. Results from EQA can reflect real-life performance and is therefore an excellent tool to evaluate not just the individual participants' performance, but also the field analytical quality of POCT methods [3].

Noklus is a nonprofit organization and has offered EQA schemes for POCT since 1992 [4]. However, EQA is only one part of the total quality improvement system

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offered by Noklus; the organization offer participants guidance and education through site visits, telephone consultations and courses, gives advice about what instruments to buy, and provides EQA schemes for most of the analytes used in primary healthcare. Participation in Noklus is not mandatory; nevertheless, 99% of all general practitioner (GP) offices and 96% of all nursing homes in Norway participate, in addition to other participants in primary care (home care, prisons, oil platforms, etc.), and Norwegian hospitals; altogether more than 3100 participants.

For $HbA_{1c}$, Noklus has about 1500 participants from both hospitals and primary healthcare. A commutable EDTA whole blood material is circulated and target values are set by reference measurement methods, meaning that the trueness of all $HbA_{1c}$ methods on the Norwegian market is evaluated and monitored. Because the participants analyze the samples in duplicate, we are also able to calculate and monitor the precision of the measurement methods. In addition, we always ask for the reagent lot number used in each EQA scheme for all components, meaning that the lot-to-lot variation is possible to monitor. Such information has been reported to be critical for the correct interpretation of the participant performance [5]. Furthermore, each time we ask for several participant performance characteristics, meaning that we can evaluate which of these factors predict good performance [6].

The aim of this study was to use EQA data to evaluate the field analytical performance of the Afinion $HbA_{1c}$ system in general practice offices against predefined performance specifications. In addition, we investigated which predictors that were associated with good participant performance.

# Materials and methods

## EQA control samples and number of participants

Noklus provides four EQA $HbA_{1c}$ surveys per year to both hospital laboratories and to POCT users. Results from the seven surveys in 2017–2018 were included in this study. The last survey in 2018 (4-2018) was not included because in Norway, the $HbA_{1c}$ units were changed from % (NGSP unites) to mmol/mol (IFCC SI units) in the period between survey 3-2018 and 4-2018. Results from surveys before 2017 were not included because the manufacturer of Afinion™ (Abbott, USA) released an improved $HbA_{1c}$ assay software for the Afinion analyzer from 2017. The total number of participants in the seven Noklus EQA surveys is shown in Table 1 together with the number of participants using the Afinion system (Alere Afinion AS100 Analyzer, Afinion 2). The Afinion participants were from primary health care only, mainly GP offices (95%).

For each EQA survey, the participants received two samples of 500 µL in two levels. The material was freshly drawn pooled EDTA whole blood from eight to 10 persons with and without diabetes. The samples were distributed by ordinary post mail. The participants were instructed to store the samples at 4 °C, to make sure that the samples reached room temperature before analysis, to analyze the samples in duplicate, preferably on two consecutive days, and to report the results within 1 week. For more details about the Noklus $HbA_{1c}$ EQA scheme, see Solvik et al. [7].

## Participant characteristics

For every EQA survey, independent of the analyte in question, Noklus always asks the participant to report information about which instrument and reagent lot number they used, the profession of the operator (in order of most to least skilled in laboratory work: biomedical laboratory scientist, medical secretary, nurse, GP/other), the number of patient samples performed per week (1–10, 11–15, 16–20, >20) and the frequency of running internal quality control (IQC) (daily/weekly, monthly, when opening a new reagent kit, never), in addition to the test result. These additional variables were used in logistic regression

**Table 1:** Number of participants in the Noklus' EQA surveys for $HbA_{1c}$, and the performance of the participants using Afinion.

| EQA survey | Total[a] | | | | | Afinion participants |
|---|---|---|---|---|---|---|
| | n | n | Response rate | Good/good n (%) | Poor ×1 n (%) | Other n (%) |
| 1-2017 | 1486 | 819 | 89.3 | 715 (97.8) | 16 (2.2) | 0 (0.0) |
| 2-2017 | 1487 | 823 | 89.4 | 726 (98.6) | 7 (1.0) | 3 (0.4) |
| 3-2017 | 1472 | 818 | 90.2 | 733 (99.3) | 4 (0.5) | 1 (0.1) |
| 4-2017 | 1476 | 821 | 91.4 | 742 (98.9) | 5 (0.7) | 3 (0.4) |
| 1-2018 | 1482 | 827 | 91.1 | 741 (98.4) | 12 (1.6) | 0 (0.0) |
| 2-2018 | 1478 | 849 | 90.7 | 764 (99.2) | 5 (0.6) | 1 (0.1) |
| 3-2018 | 1480 | 852 | 89.1 | 748 (98.6) | 10 (1.3) | 1 (0.1) |
| Sum | 10,361 | 5809 | 90.2 | 5169 (98.7) | 59 (1.1) | 9 (0.2) |

[a]Total number of participants both from primary healthcare and hospital laboratories. Good/Good, good performance on both control sample 1 and 2; Poor ×1; poor performance on at least one of the two control samples; Other, other combinations (e.g. good/no answer).

models to investigate which were associated with good participant performance.

## Stability and homogeneity

For each EQA survey the stability of the control material was examined according to ISO 13528 [8]. Examination of the homogeneity of this control material is considered irrelevant and was not performed. Examination of stability was performed at the Department of Medical Biochemistry and Pharmacology (Haukeland University Hospital, Bergen, Norway) in the following way: Two cryovials at each $HbA_{1c}$ level were first stored for 1 day at room temperature, then one vial from each level was frozen and the other vials were stored at 4 °C for 6 days and then frozen. All frozen vials were thawed and analyzed at the same time on the Variant II HPLC (Bio-Rad Laboratories) in six replicates. The material fulfilled the stability requirements [8] in all EQA surveys. In addition to this stability testing, the day-to-day stability using the participant's reported results was evaluated and accepted in each survey.

## Target values

The target value for each EQA sample was assigned by the European Reference Laboratory for Glycohemoglobin (ERL) (Winterswijk, The Netherlands), by using three IFCC secondary reference measurement procedures; (1) HA8180V, ionic exchange HPLC (Menarini), (2) Hb9210, affinity chromatography HPLC (Trinity Biotech), and (3) Capillary 2 FP, capillary electrophoresis (Sebia). The results were given in both $\%HbA_{1c}$ (DCCT/NGSP units) and mmol/mol $HbA_{1c}$ (IFCC units). In this study, the DCCT/NGSP units were used, which was in line with common practice in Norway before the last quartile of 2018. The target value was the mean of duplicate measurements from the three mentioned reference methods. The DCCT/NGSP values were derived from IFCC values using the master equation [9].

## Performance specifications

The participant performance specification of ±6% recommended by the College of American Pathologists (CAP) [10] was used in this study. This specification is based on single measurements. However, in the Noklus EQA schemes the mean of duplicate measurements is used instead of single measurements. The participant performance in this report was categorized as "good" if the mean of the duplicate measurements was within 6% of the target value, and "poor" if the result was outside these limits.

The performance of the measurement methods was evaluated against the method performance specifications of a within-laboratory CV of <2% and a between-laboratory CV of <3.5% as recommended by the National Academy of Clinical Biochemistry (NACB) [11] for methods used for diagnosis of diabetes. The specification for between-laboratory CV is also used by CAP [10]. In addition, the mean systematic deviation from the target value (bias) for the Afinion system was evaluated against the specification of bias <0.3 $\%HbA_{1c}$ used by CAP [10].

## Statistics

Before calculating the within- and between-laboratory analytical imprecision, outliers were excluded (values outside mean ± 3 SD). The number (percent) of outliers varied between 4 (0.5%) and 13 (1.8%) in the different surveys.

The participants analyzed each EQA sample in duplicate, usually on two different days. The difference between these duplicate measurements was used to estimate the pooled within-laboratory imprecision for each EQA survey, using the formula:

$$CV_{within}(\%) = \frac{\sqrt{\frac{\sum diff^2}{2n}}}{median} \cdot 100\ \%$$

where *diff* is the difference between duplicate measurements for each participant, *n* is the number of differences and *median* is the median of all duplicate means.

Before the between-laboratory variation of *single measurements* can be calculated, the between-laboratory variation for *mean of duplicate measurements* must be estimated, using the formula:

$$CV_{inter}(\%) = \frac{\sqrt{\frac{\sum(\bar{x}_i - \bar{x}_{mean\ dup})^2}{n-1}}}{median} \cdot 100\%$$

based on duplicate measurements

where $\bar{x}_i$ is the mean of duplicate measurements for each participant, $\bar{x}_{mean\ dup}$ is the mean of the duplicate measurements for all participants, *n* is the number of participants, and *median* is the median of all duplicate means.

The between-laboratory variation based on single measurements was calculated for each EQA survey using the formula:

$$CV_{between}(\%) = \sqrt{CV_{inter}^2 + \frac{CV_{within}^2}{2}}$$ based on single measurements

Logistic regression analyses were used to investigate which factors were associated with good participant performance. The outcome (dependent variable) was the participant performance with the two categories "good" and "poor" performance. Good performance was defined as results within the performance specification on *both* controls (sample 1 and 2) in an EQA survey (good/good). Poor performance was defined as results outside the performance specifications on at least one of the two control samples (poor/good, good/poor and poor/poor). The categorical predictors (independent variables) were the above-mentioned variables describing the participants and the reagent lot numbers used. The logistic regression analysis was performed for each EQA survey separately and for all seven surveys combined. In the latter analysis, kit reagent lot numbers used by less than 20 participants and missing lot numbers were grouped in a separate category. The kit reagent lot number with the highest number of participants was used as reference category. p-Values <0.05 were considered statistically significant. IBM SPSS Statistics 25.0 was used to perform the logistic regression analyses.

Student's t-test was used to evaluate differences between kit reagent lot numbers in each survey, and p-values <0.01 were considered statistically significant. The median value for lot numbers used by five or more participants were included in the evaluation.

# Results

## Participant performance

The response rate was about 90% in all seven EQA surveys (Table 1). The overall pass rates for the Afinion users, i.e. the percentage of participants within the performance specifications of ±6%, varied from 98.2% to 99.7% for each control sample in each EQA survey, and from 97.8% to 99.3% when the two control samples were combined (both passing) in the different EQA surveys (Table 1). The distribution of participant results in relation to the performance specifications is illustrated in Youden plots for each EQA survey in Supplementary Figure 1.

## Factors that predicted good participant performance

Predictors that were associated with good participant performance for the Afinion users were different in the different surveys, meaning that no predictor was constantly associated with good participant performance more than once when performing logistic regression analysis for each EQA survey separately. Several groups had no participants with poor performance in each EQA survey, meaning that the odds ratios could not be calculated (zero cells).

When pooling results from all seven EQA surveys, the factors "Frequency of internal QC" and "Kit reagent lot number" were associated with good performance (Table 2). Performing internal QC monthly was associated with better performance than using daily/weekly internal QC. Five lot numbers were associated with poorer results than the other reagent lots (odds ratio lower than 1) (Table 2). Five other lot numbers had no participants with poor performance (Table 2).

## Measurement method performance

All $HbA_{1c}$ measurement methods used in primary healthcare and hospitals in Norway fulfilled the recommended requirements for bias for all samples in all EQA surveys (Figure 1). The pooled within-laboratory CV was less than 2% for all measurement methods, except for the POCT Quo-Test $A_{1c}$ which had CV > 2% in nine of 14 control samples (Figure 1).

For the Afinion system, the pooled within-laboratory CV varied from 1.3% to 1.5%, the between-laboratory CV varied from 1.5% to 2.1%, and the systematic deviation from the reference target value (bias) varied between −0.17 and −0.01 $HbA_{1c}$% in all surveys (Table 3).

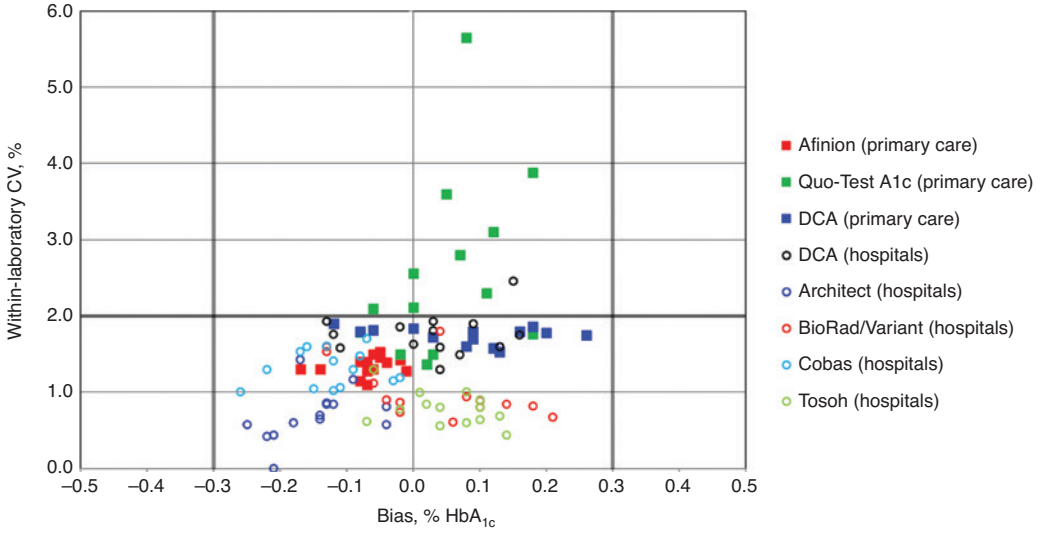


**Figure 1:** Pooled within-laboratory CV and mean systematic deviation from the target value (bias) in relation to the recommended performance specifications (gray lines) for the most commonly used $HbA_{1c}$ measurement methods in primary care and hospitals in Norway. Results from seven $HbA_{1c}$ EQA surveys in 2017–2018 (14 samples in total). n = average number of participants in the surveys. Afinion (n = 724): Alere Afinion AS100 Analyzer/Afinion 2; DCA (n = 459 primary care, n = 25 hospitals): DCA 2000/2000 + /Vantage; Architect (n = 6): Architect c4000/c8000/ci8200 (Tina-quant); BioRad/Variant (n = 9): BioRad D10/D100/Variant II Turbo (HPLC); Cobas (n = 20): Cobas c501/c502, Cobas Integra 400/400 Plus/800 (Tina-quant); Tosoh (n = 13): Tosoh G7/G8/G11 (HPLC); Quo-Test $A_{1c}$ (n = 12).

**Table 2:** Logistic regression analysis for all seven EQA surveys combined for Afinion $HbA_{1c}$.

| Predictors | | | Odds ratio (95% CI) |
|---|---|---|---|
| Profession of the operator | | | |
| Medical secretary (n = 4158) | | | 1 (ref) |
| Biomedical laboratory scientist (n = 268) | | | 3.9 (0.5–29) |
| Nurse (n = 602) | | | 1.4 (0.5–3.6) |
| GP and others (n = 121) | | | 0.8 (0.2–3.4) |
| No answer (n = 79) | | | 0.3 (0.1–1.2) |
| Number of $HbA_{1c}$ analyses performed per week | | | |
| 1–10 (n = 1744) | | | 1 (ref) |
| 11–15 (n = 854) | | | 0.8 (0.4–1.9) |
| 16–20 (n = 677) | | | 0.8 (0.3–1.7) |
| > 20 (n = 1888) | | | 1.2 (0.6–2.4) |
| No answer (n = 65) | | | 0.3 (0.1–1.2) |
| Frequency of internal QC | | | |
| Daily/weekly (n = 2905) | | | 1 (ref) |
| Monthly (n = 1174) | | | **2.7 (1.1–6.6)**[a] |
| When opening a new reagent kit (n = 382) | | | 1.2 (0.4–3.1) |
| Never (n = 181) | | | 0.7 (0.2–2.5) |
| No answer (n = 586) | | | 1.3 (0.6–3.1) |
| **Kit reagent lot number** | **Lot code** | **Exp. date** | |
| 10193607 (n = 666) | 21 | 10.2019 | 1 (ref) |
| 10196709 (n = 155) | 27 | 05.2020 | 0.8 (0.1–7.4) |
| 10195679 (n = 251) | 26 | 03.2020 | 0.4 (0.1–1.8) |
| 10195436 (n = 70) | 25 | 02.2020 | NPP[b] |
| 10195320 (n = 134) | 24 | 02.2020 | 0.6 (0.1–5.7) |
| 10194835 (n = 232) | 23 | 01.2020 | 0.3 (0.1–1.2) |
| 10194033 (n = 221) | 22 | 11.2019 | 0.3 (0.1–1.7) |
| 10190990 (n = 131) | 20 | 09.2019 | **0.1 (0.03–0.5)**[a] |
| 10190590 (n = 431) | 19 | 08.2019 | 0.4 (0.1–1.6) |
| 10190252 (n = 397) | 18 | 06.2019 | 0.6 (0.1–3.1) |
| 10189769 (n = 29) | 17 | 06.2019 | NPP[b] |
| 10189349 (n = 389) | 16 | 05.2019 | 0.6 (0.1–3.0) |
| 10188585 (n = 116) | 15 | 03.2019 | 0.5 (0.1–4.9) |
| 10188397 (n = 149) | 14 | 03.2019 | NPP[b] |
| 10187455 (n = 29) | 13 | 02.2019 | NPP[b] |
| 10186921 (n = 198) | 12 | 12.2018 | 0.4 (0.1–2.6) |
| 10186147 (n = 380) | 11 | 11.2018 | 1.6 (0.2–16) |
| 10185926 (n = 124) | 10 | 11.2018 | 0.6 (0.1–5.4) |
| 10185511 (n = 319) | 9 | 10.2018 | **0.2 (0.6–0.9)**[a] |
| 10184794 (n = 34) | 8 | 09.2018 | NPP[b] |
| 10184364 (n = 145) | 7 | 07.2018 | **0.2 (0.04–0.8)**[a] |
| 10183704 (n = 36) | 6 | 07.2018 | **0.03 (0.01–0.12)**[a] |
| 10183343 (n = 68) | 5 | 06.2018 | 0.3 (0.03–3.0) |
| 10182328 (n = 81) | 4 | 03.2018 | 0.3 (0.03–3.2) |
| 10179727 (n = 22) | 2 | 09.2017 | **0.02 (0.004–0.11)**[a] |
| No answer/n < 20 (n = 220)[c] | | | 0.5 (0.1–3.2) |

[a]Odds ratio different from 1, $p < 0.05$. [b]NPP, no poor performance. [c]Lot number not reported (no answer), or lot numbers used by less than 20 participants. Odds ratio (95% CI) for different predictors of good participant performance.

## Afinion reagent lot-to-lot variation

A total of 28 different kit reagent lot numbers were used by n ≥ 5 Afinion participants in the seven EQA surveys (Supplementary Tables 1–7). Statistically significant differences between some of the reagent lots were detected in all surveys. However, the maximum deviation between two lot numbers in each survey was less than 0.2 %$HbA_{1c}$. Statistically significant differences from the target value were found for 58% of the reagent

**Table 3:** The within and between-laboratory CV and bias for the Afinion $HbA_{1c}$ for each control sample in each EQA survey.

| EQA survey | Sample | Target value (%$HbA_{1c}$) | n[a] | Bias (%$HbA_{1c}$) | CV-within (95% CI) | CV-between (95% CI) |
|---|---|---|---|---|---|---|
| 1-2017 | 1 | 5.96 | 715 | −0.06 | 1.3 (1.24, 1.37) | 1.8 (1.76, 1.95) |
| | 2 | 7.07 | 712 | −0.17 | 1.3 (1.22, 1.35) | 1.8 (1.75, 1.94) |
| 2-2017 | 1 | 5.52 | 707 | −0.02 | 1.4 (1.34, 1.49) | 1.8 (1.71, 1.90) |
| | 2 | 6.22 | 703 | −0.07 | 1.4 (1.33, 1.48) | 1.9 (1.79, 1.99) |
| 3-2017 | 1 | 5.25 | 720 | −0.05 | 1.5 (1.46, 1.61) | 2.0 (1.92, 2.13) |
| | 2 | 6.44 | 714 | −0.04 | 1.4 (1.32, 1.47) | 1.9 (1.79, 1.98) |
| 4-2017 | 1 | 6.12 | 729 | −0.07 | 1.3 (1.22, 1.35) | 1.8 (1.67, 1.85) |
| | 2 | 6.98 | 723 | −0.08 | 1.2 (1.09, 1.21) | 1.7 (1.67, 1.85) |
| 1-2018 | 1 | 5.01 | 729 | −0.06 | 1.5 (1.45, 1.60) | 1.8 (1.76, 1.95) |
| | 2 | 6.24 | 726 | −0.14 | 1.3 (1.24, 1.37) | 1.8 (1.68, 1.86) |
| 2-2018 | 1 | 5.48 | 749 | −0.08 | 1.4 (1.30, 1.44) | 2.0 (1.86, 2.06) |
| | 2 | 7.72 | 744 | −0.07 | 1.1 (1.06, 1.17) | 1.5 (1.45, 1.60) |
| 3-2018 | 1 | 5.00 | 734 | −0.05 | 1.5 (1.39, 1.54) | 2.1 (1.98, 2.19) |
| | 2 | 6.76 | 731 | −0.01 | 1.3 (1.22, 1.35) | 1.7 (1.59, 1.76) |

[a]After exclusion of outliers. CI, confidence interval.

lots, but all lots were within the bias specification of 0.3 %$HbA_{1c}$ (Figures 2 and 3); the maximum deviation for one lot was 0.32 %$HbA_{1c}$ (lot code 6, lot number 10183704, control sample 2, 1-2017) (Figure 2).

When a lot number was used in several EQA surveys (e.g. lot codes 4 and 9 which represent lot numbers 10185511 and 10182328, respectively), these lots had approximately the same deviation from the target value in all surveys (Figures 2 and 3).

## Discussion

In this study we evaluated the analytical performance of POC $HbA_{1c}$ measurement methods used in primary health care in Norway, with special emphasis on the performance of the Afinion. It is currently debated whether POC $HbA_{1c}$ instruments have the sufficient analytical quality for diagnosis and management of patients with diabetes mellitus [11]. In a laboratory study, it has been shown that some of the POC measurement methods fulfilled the criteria for this purpose [12]. It is, however, also important to examine the quality of such instruments in "real life". In this field study, we found that the Afinion measurement system had similar analytical quality as the hospital laboratory measurement methods and that they fulfilled the analytical performance specifications for bias and imprecision in the hands of the users. This confirms the findings in a previous paper [7].

Each participant in the Noklus EQA scheme for $HbA_{1c}$ was evaluated against the performance specification of total allowable deviation ±6% [10]. The overall pass rate for Afinion users was more than 98%, meaning that the participant performance was very good. The fact that the Afinion users participate in the Noklus total quality improvement system may have affected the quality in a positive way. It has been shown that participating in a quality management system with support from laboratory medicine professionals, will improve the quality of the POCT results [6, 13]. It might be argued that the high pass rate is because only the "good participants" report EQA results. However, as 99% of GP offices participate in Noklus, the response rate was about 90% in all seven surveys, and the non-responders were random (no consistency), the results can be considered reliable.

Many factors can influence the quality of POC results [6]. In our study, we investigated which independent factors predict good analytical performance of Afinion $HbA_{1c}$ measurements. When pooling results from all seven surveys, the factor "reagent lot number" was associated with good participant performance (Table 2). The finding that performing internal QC monthly was associated with better performance than using daily/weekly QC should be interpreted with care as it is of borderline statistical significance and could be a random finding. Factors like profession of the operator and the number of $HbA_{1c}$ analyses performed per week were not shown to influence the measurement quality. From the reagent lot evaluation in this study it seems like the newer lots are better than the old. Four out of the five lots that were associated with poorer results (Table 2) were used in the beginning of 2017, and from the third survey in 2018 only "good" lots were on the market. This indicates that the quality has improved

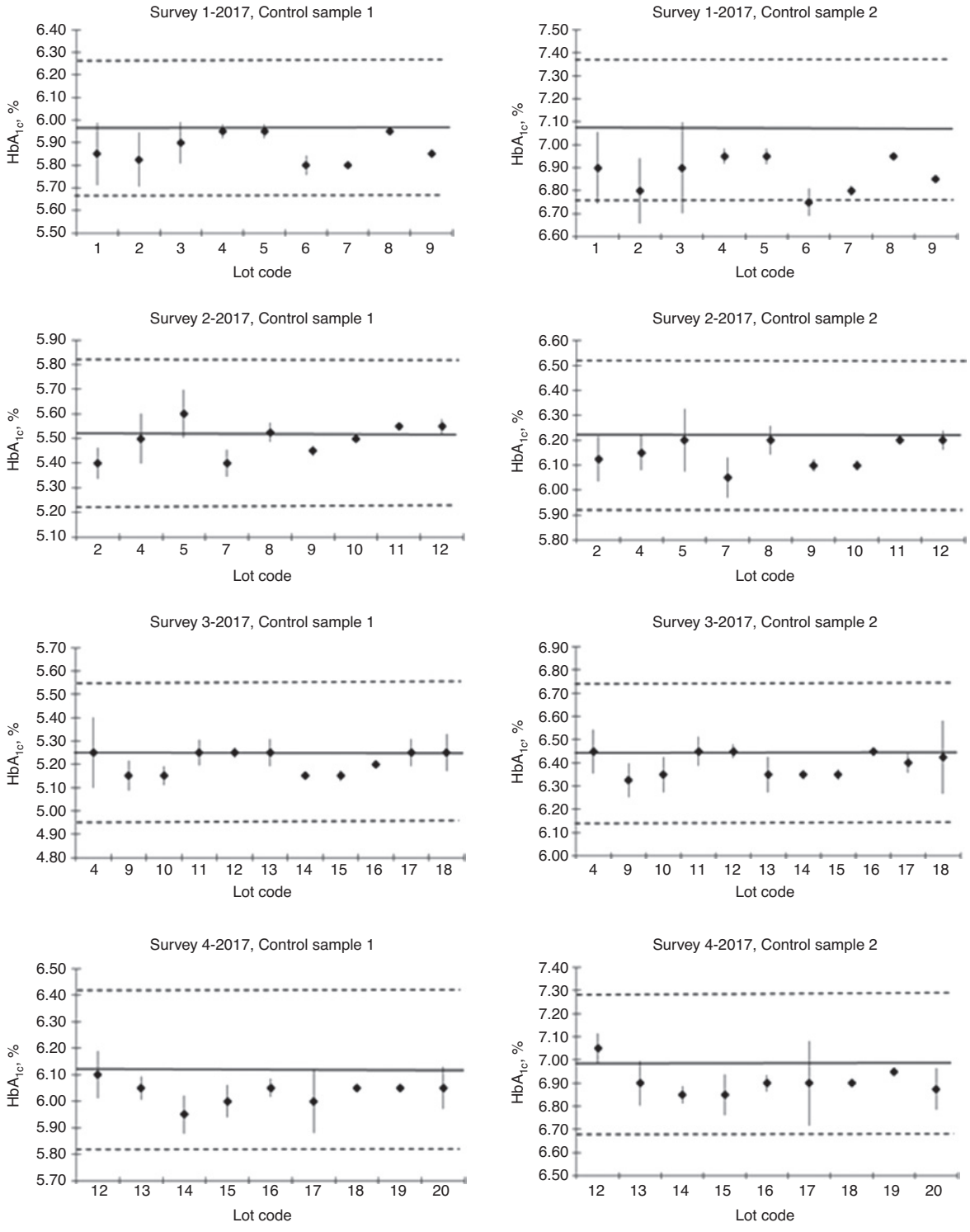


**Figure 2:** Median $HbA_{1c}$ values with 99% CI for each Afinion kit reagent lot number for control sample 1 and 2 in the 2017 EQA surveys. The horizontal solid lines represent the target value, the dotted lines the performance specification for acceptable bias (±0.3 %$HbA_{1c}$).

over time. This is also reported in a recent study from Sweden in which they show that the analytical quality of Afinion has increased over the years, now showing equal quality to hospital measurement methods [14].

In our study, we evaluated the bias and imprecision of different $HbA_{1c}$ measurement methods commonly used by hospital laboratories and primary health care in Norway. All methods, except the POCT Quo-Test $A_{1c}$, fulfilled the

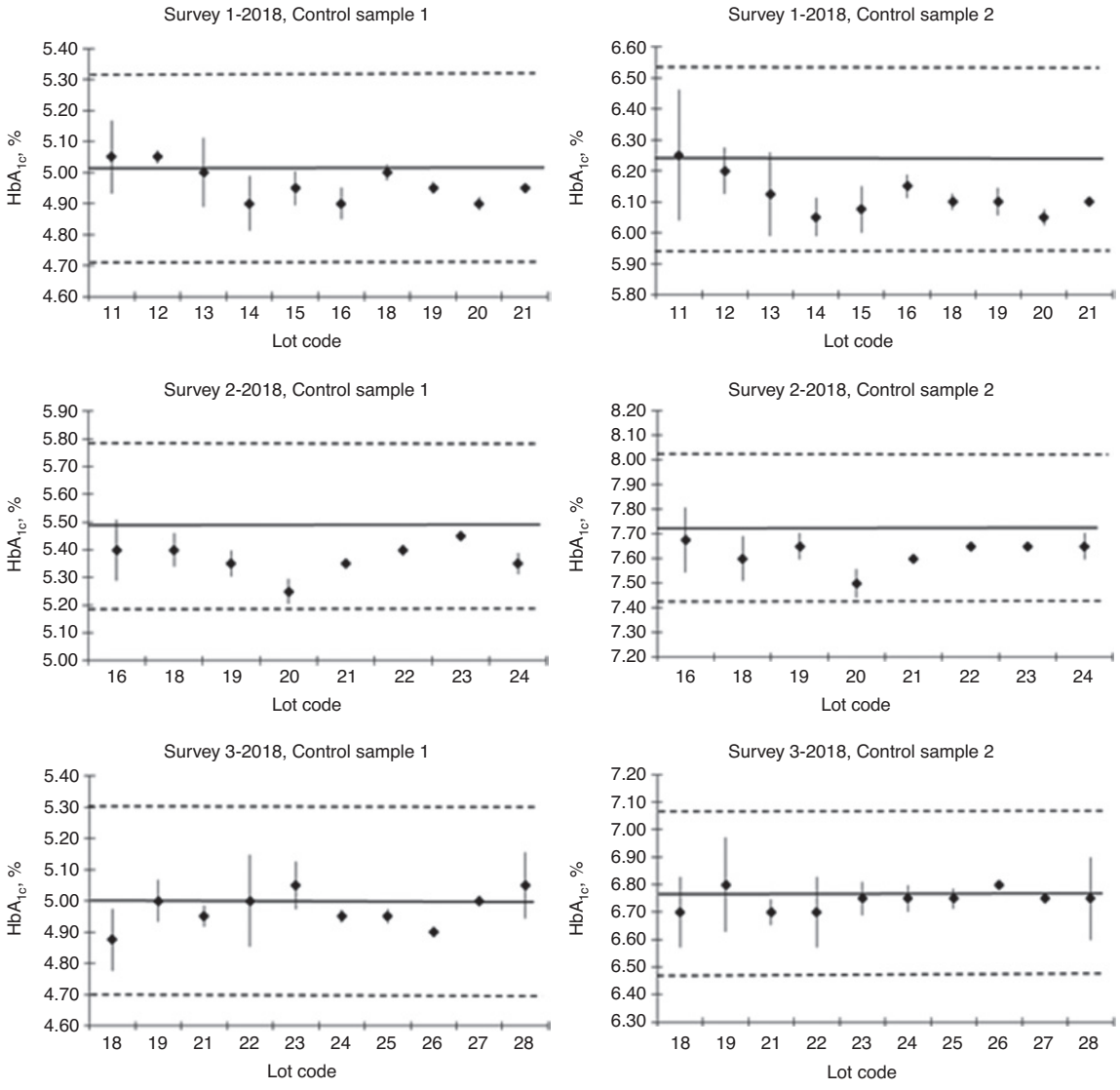


**Figure 3:** Median $HbA_{1c}$ values with 99% CI for each Afinion kit reagent lot number for control sample 1 and 2 in the 2018 EQA surveys. The horizontal solid lines represent the target value, the dotted lines the performance specification for acceptable bias (±0.3 %$HbA_{1c}$).

analytical performance specifications. Even if the $HbA_{1c}$ measurement methods fulfilled the specification for imprecision, it is important to notice that the CVs in this study are an expression of the *pooled* within-laboratory variation and not an expression of the imprecision in *each* laboratory. This means that even if a $HbA_{1c}$ measurement method has a CV below the criteria, some laboratories with this method can have larger CVs. Also, EQA results do not consider the uncertainty caused by pre-analytical factors, like, for example, blood sampling. In our study, the pooled within-laboratory CV for Afinion varied from 1.3% to 1.5% in each survey, while in a single center study with one reagent lot only, the Afinion system achieved an imprecision CV <1.2% [12]. The CAP 2018 results showed that the Afinion had a bias between −0.18 and 0.05 %$HbA_{1c}$ in the different surveys (15 samples in total) [10] which is in line with our results (Table 3). The European $HbA_{1c}$ Trial showed a bias of −0.06% $HbA_{1c}$ and a between-laboratory CV of 2.2% for the Afinion system [15], which are in line with the findings in our study.

In conclusion, the Afinion $HbA_{1c}$ has an analytical quality that fulfills the performance specifications and is robust in the hands of the users. Therefore, it can be used in diagnosing and monitoring patients with diabetes, given that the instruments are monitored by an EQA system and that the operators participate in a total quality system for POCT. In the present study, reagent lot was an independent factor to predict good participant performance. Even if the Afinion reagent lot-to-lot variation was low, it is important to continue monitoring lots in EQA schemes in the future [5].

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