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## Availability and analytical quality of hemoglobin A<sub>1c</sub> point-of-care testing in general practitioners' offices are associated with better glycemetic control in type 2 diabetes

<https://doi.org/10.1515/cclm-2020-0026>

Received January 10, 2020; accepted February 17, 2020; previously published online March 25, 2020

### Abstract

**Background:** It is not clear if point-of-care (POC) testing for hemoglobin A<sub>1c</sub> (HbA<sub>1c</sub>) is associated with glycemetic control in type 2 diabetes.

**Methods:** In this cross-sectional study, we linked general practitioner (GP) data on 22,778 Norwegian type 2 diabetes patients to data from the Norwegian Organization for Quality Improvement of Laboratory Examinations. We used general and generalized linear mixed models to investigate if GP offices' availability (yes/no) and analytical quality of HbA<sub>1c</sub> POC testing (average yearly "trueness score", 0–4), as well as frequency of participation in HbA<sub>1c</sub> external quality assurance (EQA) surveys, were associated with patients' HbA<sub>1c</sub> levels during 2014–2017.

**Results:** Twenty-eight out of 393 GP offices (7%) did not perform HbA<sub>1c</sub> POC testing. After adjusting for

confounders, their patients had on average 0.15% higher HbA<sub>1c</sub> levels (95% confidence interval (0.04–0.27) (1.7 mmol/mol [0.5–2.9])). GP offices participating in one or two yearly HbA<sub>1c</sub> EQA surveys, rather than the maximum of four, had patients with on average 0.17% higher HbA<sub>1c</sub> levels (0.06, 0.28) (1.8 mmol/mol [0.6, 3.1])). For each unit increase in the GP offices' HbA<sub>1c</sub> POC analytical trueness score, the patients' HbA<sub>1c</sub> levels were lower by 0.04% HbA<sub>1c</sub> (–0.09, –0.001) (–0.5 mmol/mol [–1.0, –0.01])).

**Conclusions:** Novel use of validated patient data in combination with laboratory EQA data showed that patients consulting GPs in offices that perform HbA<sub>1c</sub> POC testing, participate in HbA<sub>1c</sub> EQA surveys, and maintain good analytical quality have lower HbA<sub>1c</sub> levels. Accurate HbA<sub>1c</sub> POC results, available during consultations, may improve diabetes care.

**Keywords:** glycemetic control; hemoglobin A<sub>1c</sub>; point-of-care testing; primary care; type 2 diabetes.

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## Introduction

In diabetes, good glycemetic control and aggressive treatment of cardiovascular risk factors reduce the risk of macro- and microvascular complications [1, 2]. It has been debated whether hemoglobin A<sub>1c</sub> (HbA<sub>1c</sub>) point-of-care (POC) testing, defined as "any form of laboratory testing that takes place outside of the conventional or central laboratory" [3], can improve glycemetic control in diabetes. POC testing has the advantage of producing a test result within minutes. While a 2011 systematic review and meta-analysis concluded there was absence of evidence for the effectiveness of POC testing for HbA<sub>1c</sub> in diabetes management [4], more recent reviews have concluded that HbA<sub>1c</sub> POC testing does lower HbA<sub>1c</sub> levels, presumably by allowing the patient and doctor to discuss the test result during the visit, which can lead to changes in treatment without delay, enhance compliance, and motivate for lifestyle changes [5, 6]. The underlying evidence, however, is somewhat scarce. Some studies find no effect of POC [7, 8]. Others are small [9] or short-term randomized controlled trials [10, 11] investigating initial effects of introducing

POC testing. Others are set in countries with limited resources or lack of universal health care [12, 13], where HbA<sub>1c</sub> levels are generally high. Any effects of POC testing in such settings may not be generalizable.

In Norway, primary health care is usually provided by small groups of general practitioners (GPs) working together, sharing personnel and laboratory facilities (GP offices). Since the country is sparsely populated, transportation of blood samples to central laboratories can be challenging. POC testing, however, is widely available for a variety of analytes, including HbA<sub>1c</sub> for diagnosis and follow-up of patients with diabetes. The Norwegian Organization for Quality Improvement of Laboratory Examinations (Noklus) has provided quality systems for POC testing in primary care since 1992 [14]. In addition to education, site visits, and instrument evaluations, Noklus offers external quality assurance (EQA) schemes for many analytes. The analytical quality of POC testing improves over time with Noklus participation [15, 16], and for several HbA<sub>1c</sub> POC instruments, the analytical quality in primary care has been shown to be comparable to that of hospital laboratories [17].

By linking data from Noklus with data on more than 20,000 patients with type 2 diabetes, our aim was to investigate whether availability of HbA<sub>1c</sub> POC testing in GP offices was associated with glycemc control. In addition, we aimed to investigate if participation in HbA<sub>1c</sub> EQA surveys and analytical quality of the HbA<sub>1c</sub> POC testing were associated with the patients' HbA<sub>1c</sub> levels, which, to our knowledge, has not previously been investigated.

## Materials and methods

### Data sources

The Norwegian Diabetes Register for Adults was established in 2006 as a consent-based national quality registry [18]. It is updated annually and collects information on test results, treatments, procedures, and vascular complications by extracting data from patients' electronic medical records. During 2014–2017, more than 19,000 patients with type 2 diabetes followed up by GPs were registered on at least one occasion.

The ROSA 4 study is a collaboration between Noklus, Stavanger University Hospital, Nordland Hospital in Bodø, and the Universities of Bergen and Oslo. The study is the fourth wave of a population-based, cross-sectional multi-center study to assess the quality of diabetes care in general practice in Norway [19]. GPs in five geographically diverse Norwegian counties were invited to participate, and a total of 282 GPs in 77 GP offices agreed to contribute data. Information on test results, treatments, procedures, and vascular complications from 2014 was extracted from approximately 11,500 diabetes patients' electronic medical records by trained study nurses.

Noklus is a national nonprofit foundation which has provided quality systems, including EQA schemes, to laboratories in Norway since 1992 [14]. In 2018, Noklus had 1690 participating GP offices (99% national participation rate). Noklus has detailed information on which EQA schemes each GP office subscribes to, which POC equipment they use, and analytical quality over time.

### Study population and study variables

Data from The Norwegian Diabetes Register for Adults and the ROSA 4 study were collected using almost identical procedures. To ensure comparability in time, we used data from the registry collected during 2014–2017. We used one record per patient – the most recent where an HbA<sub>1c</sub> result was included. There was a substantial overlap between patients registered in the two data sources. When we had data on a patient from both sources, and from the same year, we used the data from ROSA 4. For each patient, we extracted information on year of birth, sex, years since diagnosis, smoking status, ethnicity, body mass index (BMI), HbA<sub>1c</sub> level, when they last had a monofilament test performed (a simple screening test designed to detect possible or definite peripheral neuropathy, a risk factor for diabetic foot ulcers), and most recent referral to an ophthalmologist.

Noklus offers four HbA<sub>1c</sub> EQA surveys per year, and both GP offices and hospital laboratories participate. For details on EQA materials, target values, etc., see Solvik et al. [17]. In short, for each EQA survey, the participants receive two samples of 500 µL (two levels: normal and elevated) of freshly drawn pooled EDTA whole blood from 8 to 10 persons with and without diabetes. The target value for each sample is assigned by the European Reference Laboratory for Glycohemoglobin (Winterswijk, The Netherlands). EQA participants analyze each sample in duplicate, usually on consecutive days. Noklus evaluates EQA participant performance as “good”, “acceptable”, or “poor” based on pre-defined algorithms (for details, see Supplementary Methods). During the study period, the HbA<sub>1c</sub> unit used by Norwegian laboratories was % HbA<sub>1c</sub> (NGSP units).

If a GP office subscribed to the HbA<sub>1c</sub> EQA program a given year, we assumed that the patients' HbA<sub>1c</sub> levels had been measured using their POC instrument. To differentiate analytical quality, we constructed a “trueness score” based on EQA participant performance, awarding a score of 2 for a good result, 1 for an acceptable result, and 0 for a poor result. A score of 0 was also given if precision was considered too poor to allow evaluation of trueness. Since each survey had two levels, and there were four surveys in a year, a maximum yearly score of 16 could be achieved. We adjusted the score by dividing it by the participant's actual number of HbA<sub>1c</sub> EQA survey participations that year (1–4). Thus, a maximum trueness score of 4 could be achieved, and a minimum of 0.

We also calculated trueness scores for other POC analyses performed by many GP offices, namely urine albumin-creatinine ratio, CRP and hemoglobin, for which twice-yearly EQA surveys are offered by Noklus.

### Statistical methods

Since patients treated by the same GP on average receive more similar care than patients treated by different GPs, and GPs

working together probably practice medicine more similarly than GPs working in different environments, we used general and generalized linear mixed models to analyze the data and account for clustering. Random effects (random intercepts) were allowed for each GP office, and for each GP within a GP office. The patient's individual characteristics were used as level 1 fixed effects, the GP characteristics as level 2 fixed effects, and the GP office characteristics as level 3 fixed effects. All statistical analyses were performed using R version 3.5.1 ([www.r-project.org/about.html](http://www.r-project.org/about.html)) with packages “tidyverse” and “lme4”.

Our main outcome measure was individual patient HbA<sub>1c</sub> levels, and our exposures were (i) if the GP office performed HbA<sub>1c</sub> POC testing (yes/no), and in the subset that did; (ii) the frequency of HbA<sub>1c</sub> EQA survey participations in a year (1–2, 3, or 4 [reference]); and (iii) average yearly trueness score (0–4). The final two exposures were investigated simultaneously in the same models. Thus, all patients who had their HbA<sub>1c</sub> level recorded the same year, and who were followed up by GPs working together in the same GP office, had the same exposures. We adjusted for the following potential confounders in the models: patient age (in years), years since diagnosis, sex, smoking status (daily smoker vs. not), ethnicity (non-European vs. European), proportion of female type 2 diabetes patients for a GP, and where relevant also type of POC instrument (“Afinion” [by Abbott, reference], “DCA” [by Siemens] or other).

Similarly, we investigated if POC testing for urine albumin-creatinine ratio, CRP, and hemoglobin were associated with HbA<sub>1c</sub> levels. Also, we investigated if HbA<sub>1c</sub> POC testing was associated with whether the recommended monofilament test had been performed the same year as HbA<sub>1c</sub> was measured, or the previous year (yes/no), and if the patient had been referred to an ophthalmologist the same year as HbA<sub>1c</sub> was measured, or during the previous 1–2 years (yes/no).

To check for interactions, we included interaction terms between exposures and other potential explanatory variables in the models, as well as a variable indicating patient data source (Diabetes Register or ROSA 4 study). Interaction terms with a p-value of <0.10 assessed by likelihood ratio tests when comparing models with and without the interaction term were further evaluated by stratification.

The analyses were pre-specified and performed according to plan.

## Ethical considerations

The study protocol was approved by the Western Norway Regional Ethical Committee (2018/1778/REK Vest).

## Results

We received data on 19,336 type 2 diabetes patients from the Diabetes Register for Adults and 10,356 from the ROSA 4 study. After removing records lacking an HbA<sub>1c</sub> result, or with HbA<sub>1c</sub> recorded prior to 2014, duplicates (individuals present in both data sources), and records lacking information on GP, we had information on 22,778 unique

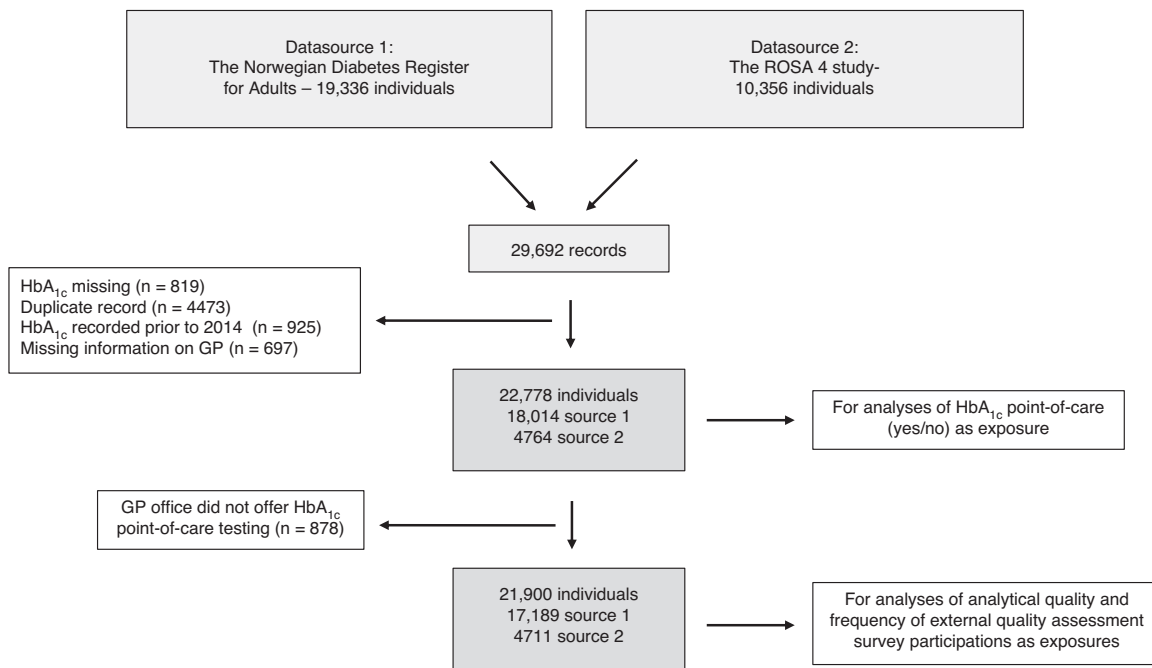
individuals with type 2 diabetes followed up in primary care, who had had their HbA<sub>1c</sub> level recorded during 2014–2017 (Figure 1).

A total of 1267 GPs from 393 GP offices contributed data to the Diabetes Register and/or the ROSA 4 study (Table 1). Patients from the registry were on average older, had a longer diabetes duration, were more likely to be of European origin, and less likely to be daily smokers than patients from the ROSA 4 study. Patients from the registry were also more likely to have had their BMI recorded, a monofilament test performed, and having been referred to an ophthalmologist. Women, on average, had slightly lower HbA<sub>1c</sub> levels than men (–0.08% HbA<sub>1c</sub>, 95% confidence interval [–0.11, –0.05], –0.9 mmol/mol [–1.2, –0.5]), and non-Europeans higher HbA<sub>1c</sub> levels than Europeans (0.13% HbA<sub>1c</sub> [0.08, 0.18], 1.4 mmol/mol [0.9, 2.0]) (Supplementary Table 1).

Three hundred and sixty-five out of 393 GP offices (93%) performed HbA<sub>1c</sub> POC testing, and “Afinion” (Abbott) was the most commonly used instrument (Table 1). More than 80% of GP offices participated in all four HbA<sub>1c</sub> EAQ surveys offered in a year, and median trueness score was high (3.25 of 4 in 2014 and 3.75 of 4 in 2017).

A total of 878 patients were followed up by GPs who did not perform HbA<sub>1c</sub> POC testing the year the patient's HbA<sub>1c</sub> level was recorded. Adjusted for potential confounders, these patients, on average, had 0.15% higher levels of HbA<sub>1c</sub> (0.04, 0.27) (1.7 mmol/mol [0.5, 2.9], Table 2). For the 21,900 individuals followed up by GPs who did perform HbA<sub>1c</sub> POC testing, the GP offices' frequency of HbA<sub>1c</sub> EQA participations was associated with patients' HbA<sub>1c</sub> levels. If the GP office had participated in three HbA<sub>1c</sub> EQA surveys during the year rather than four, the patients had HbA<sub>1c</sub> levels that were on average 0.05% HbA<sub>1c</sub> (0.001, 0.11) higher (0.6 mmol/mol [0.01, 1.2]). If the GP office had participated in only one or two surveys, the patients had HbA<sub>1c</sub> levels that were on average 0.17% HbA<sub>1c</sub> (0.06, 0.28) higher (1.8 mmol/mol [0.6, 3.1]). Analytical quality was also important; for each unit increase in the GP offices' analytical trueness scores, the patients' HbA<sub>1c</sub> levels were lower by 0.04% HbA<sub>1c</sub> (–0.09, –0.001) (–0.5 mmol/mol [–1.0, –0.01]).

The association between HbA<sub>1c</sub> POC testing and HbA<sub>1c</sub> level varied with smoking status (p-for interaction 0.06). When GPs performed POC testing, HbA<sub>1c</sub> levels in non-smokers were lower by 0.13 % HbA<sub>1c</sub> (0.01, 0.24) (1.4 mmol/mol HbA<sub>1c</sub> [0.1, 2.6]), while for smokers, HbA<sub>1c</sub> levels were lower by 0.25% HbA<sub>1c</sub> (0.03, 0.48) (2.8 mmol/mol [0.3, 5.3]). Effects of exposure variables did not vary by patient data source, type of POC instrument, patient sex, or ethnicity.



**Figure 1:** Study population.

## Sensitivity analyses

Since hospital laboratories also participate in Noklus HbA<sub>1c</sub> EQA surveys, we could compare analytical quality between primary care POC and hospital laboratory methods. We found no systematic differences that could explain the association between availability of POC testing and lower HbA<sub>1c</sub> levels (Supplementary Table 2 and Supplementary Figure 1).

In Noklus HbA<sub>1c</sub> EQA surveys, level 2 is above 6.5% HbA<sub>1c</sub> (48 mmol/mol). When pooling bias (participants' level 2 result minus reference value) for all EQA participants and all 16 surveys during 2014–2017, we observed that poor performers on average measured lower than the target value, rather than higher (Supplementary Figure 2). Thus, any possible systematic bias in measurements could not explain why poor performers had patients with higher HbA<sub>1c</sub> levels.

Sixty-one percent of patients had had the recommended monofilament test, and 63% had been referred to an ophthalmologist (Table 1). Whether or not the GP performed HbA<sub>1c</sub> POC testing was not associated with the patient's odds of having had a monofilament test (odds ratio [OR] 0.78, 95% CI [0.41, 1.48]) or having been referred to an ophthalmologist (OR 1.10, [0.81, 1.49]). However, for patients followed up by GPs who did perform HbA<sub>1c</sub> POC testing, the odds of having had a monofilament test increased with increasing analytical trueness score

(OR 1.18, [1.02, 1.35]), and so did the odds of having been referred to an ophthalmologist (OR 1.18, [1.06, 1.31]).

Further, we investigated if GP office participation in other POC EQA schemes was associated with patients' HbA<sub>1c</sub> levels. Frequency of participation and obtained analytical trueness score in EQA surveys for the analytes hemoglobin, CRP, or urine albumin-creatinine ratio were not associated with patients' HbA<sub>1c</sub> levels (Supplementary Table 3). However, as Noklus offers only two yearly EQA surveys for these analytes, compared to four for HbA<sub>1c</sub>, we had less statistical power to detect potential differences.

## Discussion

By novel use of validated patient data from Norwegian GPs linked with laboratory data from Noklus EQA surveys, we found that the availability of HbA<sub>1c</sub> POC testing, frequency of participation in HbA<sub>1c</sub> EQA surveys, and good analytical quality were all associated with lower levels of HbA<sub>1c</sub> in type 2 diabetes patients treated in primary care. Better analytical quality was also associated with higher patients' odds of having had a monofilament test done and having been referred to an ophthalmologist.

While some investigators have found no associations between availability of HbA<sub>1c</sub> POC testing and HbA<sub>1c</sub> levels in patients with diabetes [7, 8], many have [9–13]. These

**Table 1:** Individual- and GP office characteristics, overall and stratified by data source and year.

|   | Total            | Norwegian Diabetes Register for Adults | ROSA 4 study     |
|---|------------------|--|------------------|
| Individuals, n (%)  | 22,778 (100)     | 18,014 (79.1)                          | 4764 (20.9)      |
| GPs, n  | 1267             | 1216                                   | 278              |
| GP offices, n   | 393              | 383                                    | 76               |
| Individual patient characteristics                          |                  |  |                  |
| Median HbA <sub>1c</sub> (10–90th percentile)               |                  |  |                  |
| HbA <sub>1c</sub> , %                                       | 6.9 (5.9–8.5)    | 6.9 (5.9–8.4)                          | 6.8 (5.8–8.7)    |
| HbA <sub>1c</sub> , mmol/mol                                | 52 (41–69)       | 52 (41–68)                             | 51 (40–72)       |
| Age, years, median (10–90th percentile)                     | 67 (49–82)       | 67 (50–82)                             | 65 (47–82)       |
| Years since diagnosis                                       |                  |  |                  |
| Median (10–90th percentile)                                 | 8 (1–20)         | 9 (1–20)                               | 7 (1–18)         |
| Percent missing   | 4.0              | 3.0                                    | 8.1              |
| Percent female  | 43.7             | 43.0                                   | 46.4             |
| Percent non-European  | 12.1             | 10.5                                   | 18.5             |
| Percent daily smokers                                       | 16.2             | 15.7                                   | 18.1             |
| Body mass index (BMI)                                       |                  |  |                  |
| Median (10–90th percentile)                                 | 29.0 (23.4–36.8) | 29.0 (23.4–36.7)                       | 29.2 (23.5–38.7) |
| Percent missing   | 21.8             | 11.1                                   | 62.2             |
| Monofilament test performed, n (%)                          | 13,922 (61)      | 13,160 (73)                            | 762 (16)         |
| Referral to ophthalmologist, n (%)                          | 14,416 (63)      | 11,994 (67)                            | 2422 (51)        |
| Year of HbA <sub>1c</sub> measurement (%)                   |                  |  |                  |
| 2014  | 25.0             | 5.1                                    | 100.0            |
| 2015  | 15.6             | 19.7                                   | 0.0              |
| 2016  | 19.6             | 24.8                                   | 0.0              |
| 2017  | 39.9             | 50.4                                   | 0.0              |
| GP office characteristics 2014                              |                  |  |                  |
| Median number of GPs contributing data (10–90th percentile) | 2 (1–5)          | 2 (1–4)                                | 3.5 (1–6)        |
| HbA <sub>c</sub> POC available (%)                          | 167/176 (95)     | 100/106 (94)                           | 73/76 (96)       |
| Type of instrument (%)                                      |                  |  |                  |
| Afinion   | 112 (67)         | 70 (70)                                | 47 (64)          |
| DCA   | 55 (33)          | 30(30)                                 | 26 (36)          |
| HbA <sub>1c</sub> EQA participations (%)                    |                  |  |                  |
| 1–2   | 7 (4)            | 3(3)                                   | 4 (5)            |
| 3   | 23 (14)          | 16 (16)                                | 9 (12)           |
| 4   | 137 (82)         | 81 (81)                                | 60 (82)          |
| Median trueness score (0–4), (10–90th percentile)           | 3.25 (2.75–4.00) | 3.25 (2.75–4.00)                       | 3.5 (2.67–4.00)  |
| GP office characteristics 2017                              |                  |  |                  |
| Median number of GPs contributing data (10–90th percentile) |                  | 3 (1–5)                                |                  |
| HbA <sub>1c</sub> POC available (%)                         |                  | 238/257 (93)                           |                  |
| Type of instrument (%)                                      |                  |  |                  |
| Afinion   |                  | 128 (54)                               |                  |
| DCA   |                  | 106 (45)                               |                  |
| Other   |                  | 4 (2)                                  |                  |
| HbA <sub>1c</sub> EQA participations (%)                    |                  |  |                  |
| 1–2   |                  | 5 (2)                                  |                  |
| 3   |                  | 38 (16)                                |                  |
| 4   |                  | 195 (82)                               |                  |
| Median trueness score (0–4), (10–90th percentile)           |                  | 3.75 (3.00–4.00)                       |                  |

studies are, however, generally not directly comparable to ours. Some are randomized controlled trials (RCTs) with limited follow up time [10, 11] lacking the ability to demonstrate lasting effects. Others are conducted in lower resource settings than Norwegian primary care, where

HbA<sub>1c</sub> levels are high to begin with and a lot is to be gained from any intervention [9, 11, 12]. Also, to our knowledge, no one has previously investigated if EQA participation or the analytical quality of the POC testing is associated with patient HbA<sub>1c</sub> levels.

**Table 2:** Estimated absolute differences in patients' HbA<sub>1c</sub> levels by GP offices' availability of point-of-care (POC) testing for HbA<sub>1c</sub>, frequency of yearly HbA<sub>1c</sub> external quality assessment (EQA) survey participations, and analytical quality (trueness score).

|   | HbA <sub>1c</sub> (%) (95% CI) |                       | HbA <sub>1c</sub> (mmol/mol) (95% CI) |                       |
|---|--------------------------------|-----------------------|---------------------------------------|-----------------------|
|   | Crude <sup>a</sup>             | Adjusted <sup>b</sup> | Crude <sup>a</sup>                    | Adjusted <sup>b</sup> |
| POC for HbA <sub>1c</sub>                               |                                |                       |                                       |                       |
| Yes vs. no  | -0.12 (-0.23, -0.005)          | -0.15 (-0.27, -0.04)  | -1.3 (-2.5, -0.05)                    | -1.7 (-2.9, -0.5)     |
| Frequency of HbA <sub>1c</sub> EQA survey participation |                                |                       |                                       |                       |
| 3 vs. 4   | 0.07 (0.01, 0.12)              | 0.05 (0.001, 0.11)    | 0.8 (0.2, 1.3)                        | 0.6 (0.01, 1.2)       |
| 1–2 vs. 4   | 0.14 (0.03, 0.25)              | 0.17 (0.06, 0.28)     | 1.5 (0.3, 2.8)                        | 1.8 (0.6, 3.1)        |
| Trueness score (per unit increase, 0–4)                 | -0.03 (-0.07, 0.02)            | -0.04 (-0.09, -0.001) | -0.3 (-0.8, 0.2)                      | -0.5 (-1.0, -0.01)    |

<sup>a</sup>Accounted for clustering by GP and GP office as random intercepts in the models. <sup>b</sup>In addition to random effects, adjusted for the following fixed effects: patient age (in years), years since diagnosis, sex, smoking status (daily smoker vs. not), ethnicity (non-European vs. European), proportion of female type 2 diabetes patients, and type of POC instrument where relevant (Afinion [reference], DCA or other).

A more comparable study to ours in setting was a retrospective US observational study from 2001–2005. HbA<sub>1c</sub> levels for approximately 2500 patients in a diabetes clinic were followed before and after introduction of HbA<sub>1c</sub> POC testing [13]. Compared to 2000 patients with stable HbA<sub>1c</sub> levels who were followed-up in a family practice without HbA<sub>1c</sub> POC testing, patients in the diabetes clinic saw a significant decline in HbA<sub>1c</sub> levels, beginning 1 year after the introduction of HbA<sub>1c</sub> POC testing and still evident after 3.5 years. However, the authors did not discuss potential systematic differences between POC and hospital methods, nor was quality control of the methods described.

In our study, reflecting real-life follow up of type 2 diabetes patients in primary care, most were cared for by GPs performing HbA<sub>1c</sub> POC testing. Those who were not, however, had higher HbA<sub>1c</sub> levels. We also found that the GP offices' frequency of participation in HbA<sub>1c</sub> EQA surveys, as well as their actual analytical quality, demonstrated by the results in the HbA<sub>1c</sub> EQA surveys, were associated with their patients' HbA<sub>1c</sub> levels. The type of POC instrument used did not explain the results, nor were the effects significantly different depending on type of instrument used. We found no evidence to suggest that systematic measurement bias or differences between POC and hospital methods could explain these findings. This is supported by a 2017 meta-analysis, which did not find overall systematic differences between the two most commonly used HbA<sub>1c</sub> POC instruments in Norway and various hospital comparator methods [20]. Having high quality HbA<sub>1c</sub> POC analysis available in the GP office makes an accurate test result available during the consultation. This could be associated with lower patient HbA<sub>1c</sub> levels because it allows the patient and doctor to discuss the test result during the visit and make the correct clinical decisions and necessary adjustments together, thereby optimizing treatment.

We also observed that GP offices with good analytical quality of their HbA<sub>1c</sub> POC testing had patients who were more likely to have been screened for vascular complications in accordance with guidelines. Therefore, an alternative interpretation of our findings could be that in general, good analytical quality in the laboratory could be a marker of a well-organized GP office, where patients are more likely to be followed up according to guidelines and receive better overall care, resulting also in lower HbA<sub>1c</sub> levels. However, since we found no associations between the analytical quality of other POC tests and HbA<sub>1c</sub> levels, albeit with somewhat lower statistical power, this may be an indication that high quality HbA<sub>1c</sub> POC testing itself facilitates better diabetes care, lowering HbA<sub>1c</sub> levels.

It is indisputable that the absolute differences in HbA<sub>1c</sub> levels we detect are small. However, the risk of complications in diabetes increase with HbA<sub>1c</sub> levels, and there is no threshold value. In a population, many people subject to a small risk can generate more illness than the few people at high risk [21]. Therefore, to shift the whole population to a somewhat lower risk level (the population-based approach), may have a more substantial impact on population health than the conventional clinical high-risk approach. Thus, the clinical implications of the differences in HbA<sub>1c</sub> detected in our study could be important on a population level.

An important strength of our study is the novel use of validated patient data in combination with laboratory data from EQA surveys. This allowed strict control of the overall analytical quality of the HbA<sub>1c</sub> measurements for POC instruments as well as hospital instruments. More importantly, it means our study reflects the actual everyday care that diabetes patients in primary care in Norway receive. The results are not due to any initial effect following the introduction of an intervention, which can be the case in an RCT. Another important strength is the large

study population of more than 20,000 patients with type 2 diabetes. Also, since our exposures and outcomes were obtained from different data sources, any misclassification will be non-differential and, if anything, bias effect estimates towards the null.

One potential limitation of the study is that patients from the Diabetes Register may not be representative of the population of Norwegian type 2 diabetes patients. In 2017, approximately 15% of Norwegian GPs submitted data to the registry, and they are likely to be more interested in diabetes care, and therefore treat their patients according to guidelines. Although GPs also had to consent to participation in the ROSA 4 study, they represent a more random selection of Norwegian GPs, and hence their patients are likely to be more representative of Norwegian type 2 diabetes patients. However, in our study population, average HbA<sub>1c</sub> levels were very similar in the two data sources, as were other patient characteristics. Also, we did not find any indication of effects of exposures varying with patient data source. Therefore, combining the data sources to achieve the largest study population possible seemed reasonable.

Another potential limitation is that we had only the most recent record of HbA<sub>1c</sub> for each patient. For a subgroup of patients from the registry, there are more than one HbA<sub>1c</sub> record available. However, since HbA<sub>1c</sub> POC testing was widespread in Norwegian GP offices long before the start of the study period in 2014, it is unlikely that we would have been able to identify any substantial individual effects on HbA<sub>1c</sub> levels from introduction of HbA<sub>1c</sub> POC testing in a longitudinal study design. Finally, even though we were able to account for several possible confounders in our models, and clustering by GP and GP office, residual confounding cannot be excluded.

In conclusion, we found that GP offices' availability and good analytical quality of HbA<sub>1c</sub> POC testing, as well as participation in HbA<sub>1c</sub> EQA surveys, were all associated with better glyemic control in a large population of type 2 diabetes patients. Having an accurate HbA<sub>1c</sub> test result available during the consultation may facilitate better diabetes care.

**Author contributions:** All authors have accepted responsibility for the entire content of this submitted manuscript and approved submission.

**Research funding:** None declared.

**Employment or leadership:** None declared.

**Honorarium:** None declared.

**Competing interests:** The funding organizations played no role in the study design; in the collection, analysis, and interpretation of the data; in the writing of the report; or in the decision to submit the report for publication.

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**Supplementary Material:** The online version of this article offers supplementary material (<https://doi.org/10.1515/cclm-2020-0026>).