

Point-of-Care Testing for Hb A_{1c} in the Management of Diabetes: A Systematic Review and Metaanalysis

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BACKGROUND: The measurement of hemoglobin A_{1c} (Hb A_{1c}) is employed in monitoring of patients with diabetes. Use of point-of-care testing (POCT) for Hb A_{1c} results at the time of the patient consultation potentially provides an opportunity for greater interaction between patient and caregiver, and more effective care.

OBJECTIVE: To perform a systematic review of current trials to determine whether POCT for Hb A_{1c}, compared with conventional laboratory testing, improves outcomes for patients with diabetes.

METHODS: Searches were undertaken on 4 electronic databases and bibliographies from, and hand searches of, relevant journal papers. Only randomized controlled trials were included. The primary outcome measures were change in Hb A_{1c} and treatment intensification. Metaanalyses were performed on the data obtained.

RESULTS: Seven trials were found. There was a nonsignificant reduction of 0.09% (95% CI -0.21 to 0.02) in the Hb A_{1c} in the POCT compared to the standard group. Although data were collected on the change in proportion of patients reaching a target Hb A_{1c} of <7.0%, treatment intensification and heterogeneity in the populations studied and how measures were reported precluded pooling of data and metaanalysis. Positive patient satisfaction was also reported in the studies, as well as limited assessments of costs.

CONCLUSIONS: There is an absence of evidence in clinical trial data to date for the effectiveness of POCT for Hb A_{1c} in the management of diabetes. In future studies attention to trial design is needed to ensure appropriate selection and stratification of patients, collection

of outcome measures, and action taken upon Hb A_{1c} results when produced.

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The circulating glycohemoglobin (Hb A_{1c})⁶ level is an integrated measure of circulating glucose concentration over the previous 2–3 months, and in patients with diabetes mellitus this measurement can be used to predict both mortality and morbidity, in particular the risk of developing many of the long-term complications associated with diabetes (1–3). Monitoring of Hb A_{1c} is needed to adjust therapy accurately. The Hb A_{1c} level has been employed as a surrogate outcome measure in a number of landmark studies of the management of glycemic control (4–6) and is now an established and well-documented part of the management of diabetes (7–11).

Hb A_{1c} measurement, along with other tools such as blood glucose monitoring, is used to optimize glycemic control in newly diagnosed patients and then, once adequate levels of control have been established, to monitor compliance with therapy. Patients who are aware of their Hb A_{1c} level have lower measurement results than those who are unaware (12). Frequency of testing depends on the achieved levels of Hb A_{1c} and their variability. Although a recent audit of diabetes care in England for the period 2008–2009, which included more than 1.6 million people with diabetes, showed that >90% of patient records included an Hb A_{1c} result, only 67% of patients with type 2 diabetes and 29% of patients with type 1 diabetes had a recorded Hb A_{1c} of ≤7.5% (13). Despite widespread availability of the Hb A_{1c} test, there seem to be limitations to using it to facilitate improved glycemic control.

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⁶ Nonstandard abbreviations: Hb A_{1c}, glycohemoglobin; POCT, point-of-care testing.

A new technology is available that allows measurement of Hb A_{1c} by nursing staff in a clinic setting, at the time of a consultation (14). Such equipment can give results with an acceptable level of performance, although not all such systems are capable of delivering the required performance (14–16). Importantly, such systems can simplify the logistics of having recent results available at the time of the patient review. Hence, such point-of-care testing (POCT) may enable clinical decisions to be made by using the current Hb A_{1c} status of the patient and to be discussed as part of the patient–practitioner interaction.

We carried out a systematic review of randomized clinical trials to determine if the use of POCT for Hb A_{1c} to enable immediate feedback of results and clinical decision making leads to improved glycemic control compared with the use of a laboratory-based testing service in the management of patients with diabetes.

Methods

We used the PRISMA (Preferred Reporting Items for Systematic Reviews and Metaanalysis) statement as a guide to the conduct and reporting of the review (17); full details are provided in Appendix 1 of the Data Supplement that accompanies the online version of this article at <http://www.clinchem.org/content/vol57/issue4>.

SEARCH STRATEGY

We aimed to identify prior systematic reviews and metaanalyses on this topic. Narrative reviews were available but no systematic reviews. We searched Ovid versions of EMBASE (1980 to August 2010); MEDLINE (1980 to August 2010); the Cochrane Central Register of Controlled Trials, the Cochrane Library, August 2010; and CINAHL (1982 to August 2010). The search was limited to randomized controlled trials. The Cochrane highly sensitive search strategy was used on MEDLINE and the search filters suggested by the Scottish Intercollegiate Guideline Network were used for EMBASE and CINAHL.

The MeSH terms used were “Hemoglobin A, Glycosylated” AND “Point-Of-Care Systems.” In addition, we conducted a free text search for synonyms of Hb A_{1c} and point of care, as well as for known brand names of POCT devices. Full details of the search strategy are given in Appendix 2 of the online Supplement. We also searched for ongoing trials, and we hand-searched reference lists of all retrieved papers and narrative reviews and sought additional trials from experts in the field.

TRIAL SELECTION

Three trained reviewers (L. Al-Ansary, A. Farmer, and C.P. Price) reviewed the list of titles and abstracts independently for relevance and selected articles for further review. Inclusion criteria studies that were conducted in people with type 1 or type 2 diabetes and studies that compared the effects of using POCT with independent laboratory-based testing for Hb A_{1c}, and reports of individual patient-level outcomes including Hb A_{1c} outcomes and changes in treatment. The only eligible trial design was a randomized controlled trial. Observational studies, case reports, narrative reviews, letters to the editor, and other similar contributions were excluded. There were no age or language restrictions.

DATA ABSTRACTION

Data were individually abstracted by 2 family physicians and a clinical biochemist (L. Al-Ansary, A. Farmer, and C.P. Price) trained in critical appraisal of the literature, with consensus resolution (and disagreements resolved by discussion). The following data were abstracted from the included trials: design; methods of randomization; number of participants entered in trial; number of participants who completed the trial; characteristics of the population, including percentage of women; mean, median, and range of ages; duration of diabetes mellitus; outcomes measures; and adverse events.

The primary outcome measures sought were (a) the change in Hb A_{1c} level, (b) the change in proportion of patients with an Hb A_{1c} ≤ 7.0%, and (c) a measure of treatment intensification or change in treatment decisions (as a surrogate measure of action being taken on an Hb A_{1c} result) over the period of the trial. Additional outcome measures sought were emergency admissions, patient satisfaction as reflected in questionnaires, and costs.

QUALITY ASSESSMENT

We assessed the methodologic quality of the included studies for risk of bias by using the Cochrane guidance on preparing systematic reviews of interventions (18). The following specific criteria were included: sequence generation, allocation concealment, incomplete outcome data addressed, selective outcome reporting, and “other issues.” Blinding was not assessed, because the nature of the intervention did not allow blinding. On the basis of these quality criteria, the studies were broadly subdivided into 3 categories representing the risk of bias: low (if the 4 main criteria were met); moderate (if 1 or 2 were partly met); and high (if none were met).

DATA SYNTHESIS

We analyzed the change in mean Hb A_{1c} using inverse variance with a weighted average of the outcome measure, and a fixed-effect model. For the clustered trial (19), SDs were recalculated from SEs corrected for clustering supplied by the authors. For this trial, the number of patients who achieved target Hb A_{1c} levels was also adjusted for clustering.

Results

Of 551 citations identified from the combined searches, 146 duplicate records were excluded and 405 abstracts were screened, with 17 articles (19–35) selected for review of the full report: a summary is provided in Appendix 3 of the online Supplementary Materials. No additional articles were retrieved from hand-searching. Eight papers were subsequently excluded: 3 because the study had no control group; 2 because randomization was based on whether patients attended at baseline on odd or even days of the week; 1 because it was a retrospective study of medical records; 1 because it was a description of the technical performance of a POCT system; and 1 because the study compared 3 organizational strategies for managing diabetes and POCT was not part of any arm.

Nine published articles were reports of trials that met the eligibility criteria (19, 21, 22, 30–35). The trials reported by Stone et al. (32) and Laurence et al. (34, 35) were nested in the trials of Khunti et al. (30) and Bubner et al. (19), respectively, and their results were considered as part of the original trials. The study reported by Kennedy et al. (31) comprised 2 parallel trials of POCT for Hb A_{1c}, 1 with usual care (described as “no unsolicited contacts between visits” with use of a simple algorithm for insulin titration) and the other with active care (described as “weekly contact/monitoring” with active insulin titration); these 2 parallel trials were treated as 2 trials in the review. The main characteristics of the 7 trials that met the inclusion criteria and were selected for further analysis, are set out in Table 1.

CHARACTERISTICS OF TRIAL DESIGN, RISK OF BIAS, SETTING, AND POPULATION

Three reported trials involved only adult patients with type 2 diabetes, 2 involved a mixed population of adults with type 1 or type 2 diabetes; 1 reported trial involved adolescents with type 1 diabetes, and 1 simply identified the patients as having diabetes. The trial population size varied between 201 and 3953, and the overall proportion (intervention plus control arms) of patients who did not complete the trial varied between 1.1% and 34.4%. Details of the assessment of the risk of

bias, together with a summary, are given in Appendix 4 of the online Supplementary Materials.

Two trials were conducted in primary care settings, whereas 5 were conducted in ambulatory clinics in secondary care settings; both of the former and 2 of the latter were multicentered with randomization in all cases conducted individually in each center, except in the study by Bubner et al. (19), in which randomization was undertaken at a practice level. All of the trial reports indicated that in the POCT cohort the results of the Hb A_{1c} measurements were discussed with the patient at the time the result was generated, with the exception of the trial by Khunti et al. (30). In their report, Khunti et al. noted that “it proved difficult for surgeries [health centers] to organize their management of patients with diabetes in such a way as to maximize the benefits of using the rapid test for intervention group patients. Practices therefore often continued their follow-up in the usual way.”

ANALYTICAL METHODS AND PERFORMANCE

The DCA 2000 (Siemens Healthcare Diagnostics) benchtop system for measuring the Hb A_{1c} level was employed in 5 of the 7 trials. The analytical performance was reported in 3 studies (21, 22, 33). Agus et al. (33) reported a comparison between POCT and laboratory methods with a mean (SD) linear regression slope of 0.99 (0.01) and intercept of 0.91 (0.09) ($r = 0.94$). In a similar comparison Cagliero et al. (22) found a mean difference of 0.071 (0.582) ($r = 0.92$); the intraassay CV was 2.0% for the POCT system. Grieve et al. (21) reported only intraassay precision, which ranged between 3.3% and 4.7%, respectively, for QC samples that were within reference intervals and those that were not. In the trials reported by Kennedy et al. (31), the Metrika A1c Now (Metrika) was employed; analytical performance data were reported in another article (36) with correlation with the laboratory method giving a slope of 0.91 and intercept of 0.79 ($r = 0.72$). The authors also reported Bland–Altman analysis results in which “32% and 20% of the patients results were outside the limits of 0.75% and 1.0%, respectively.” This analysis was performed only on samples with Hb A_{1c} values between 8.0% (the inclusion criteria for the study) and 13.0% (the upper limit for results reported by the POCT system).

GLYCEMIC CONTROL

Data were reported on the change in Hb A_{1c} in the trials of Bubner et al. (19), Cagliero et al. (22), and Agus et al. (33); the results are summarized in Table 2. The results of a metaanalysis are shown in Fig. 1; the mean difference was -0.09% DCCT units (95% CI -0.21 to 0.02) with the test of heterogeneity, giving a χ^2 value of 0.84 ($P = 0.66$) and an I^2 value of 0%, with a test for overall

Table 1. Trial characteristics included in further analysis.

Trial	Population	Age, years ^a	Duration of diabetes, years	Proportion female, %	Participants/ completing study, n	Frequency of testing, months	Study period, months	Method of reporting change in Hb A _{1c} ^b	Treatment changes reported	Other outcome measures
Bubner et al. (19)	Type 1 and 2 (mixed therapies)	I = 67 (59–74) C = 66 (58–73)	>5	I = 45 C = 45	I = 1092/840 C = 721/622	NR ^c	18	Both methods	No	Patient satisfaction [Laurence et al. (34)]; estimated costs [Laurence et al. (35)]
Grieve et al. (21)	NR	NR	NR	NR	I = 302/301 C = 297/292	1	1	—	Yes	
Cagliero et al. (22)	Type 1 and 2 (insulin treated)	I = 49 (16) C = 49 (16)	NR	I = 52 C = 42	I = 100/86 C = 101/78	3	12	Mean method	No	Hypoglycemic episodes; emergency admission; outpatient visits; contact with patients
Khunti et al. (30)	Type 2	I = 65.9 (10.8) C = 65.4 (10.7)	4.0	I = 43 C = 41	I = 343/319 C = 338/319	NR	12	≤7.0% Method	No	Patient satisfaction [Shephard et al. (29)] Estimated costs
Kennedy et al. (31) ^d	Type 2 (uncontrolled on oral therapy)	I = 57 (12) C = 57 (11)	8.4 (6.4)	I = 47 C = 48	I = 1975/1363 C = 1978/1491	1.5	6	Both methods	Yes	
Kennedy et al. (31) ^e	Type 2 (uncontrolled on oral therapy)	I = 57 (11) C = 57 (12)	I = 8.7 (6.4) C = 8.6 (6.4)	I = 50 C = 51	I = 1973/1366 C = 1967/1501	1.5	6	Both methods	Yes	
Agus et al. (33)	Type 1	I = 12.33 (3.51) C = 12.91 (3.21)	NR	I = 53 C = 49	I = 111/77 C = 104/64	3	12	Both methods	Yes	

^a Data are mean (SD) except for Bubner et al. data, which uses median [IQR (interquartile range)].

^b The 2 methods used were reporting change in the mean level of Hb A_{1c} (designated by “Mean method”) and reporting change in the proportion of patients that had Hb A_{1c} levels equal to or below 7% (designated by “≤7.0% Method”).

^c NR, not recorded; I, intervention arm; C, control arm.

^d Usual cohort of Kennedy trial.

^e Active titration cohort of Kennedy trial.

Table 2. Results from studies in which the change in the mean Hb A_{1c} (% DCCT unit) over the course of the trial was reported.^a

Trial	POCT results, mean (SD)			n	Delayed results, mean (SD)			n
	Baseline	End point	Change		Baseline	End point	Change	
Agus et al. (33)	7.81 (1.13)		+0.16 (0.81)	77	7.90 (1.24)		+0.27 (1.05)	64
Bubner et al. (19) ^b	7.09 (2.09)	6.91 (1.97)	-0.18 (1.31)	840	7.34 (2.46)	7.22 (2.04)	-0.12 (1.45)	622
Cagliero et al. (22) ^c	8.67 (1.79)		-0.40 (0.65)	86	8.49 (1.59)		-0.19 (1.16)	78

^a DCCT, Diabetes Control and Complications Trial.
^b Adjusted for clustering.
^c 12-month results used.

effect $Z = 1.60$ ($P = 0.11$). It should be noted that Bubner et al. (19) reported outcome measures based on the proportion of patients with an Hb A_{1c} result $\leq 7.0\%$. In addition, these investigators used multiple imputation to impute missing values, and a noninferiority analysis. For the findings from this important study to be included in the review the investigators kindly agreed to provide the raw data, which was used in the above and following analyses (Caroline Laurence and Lisa Yelland, personal communication, February 2, 2010).

Data on the proportion of patients with Hb A_{1c} $\leq 7.0\%$ at the beginning and end of the trial were reported by Bubner et al. (19), Khunti et al. (30), Kennedy et al. (both usual and active titration arms) (31), and Agus et al. (33). The results are summarized in Table 3, and shown in a Forest plot (Fig. 2). Pooling of results and metaanalysis were not considered appropriate because of the large variability in the proportion of patients with a Hb A_{1c} $< 7.0\%$ at baseline, and the possibility of reductions in the Hb A_{1c} in some patients being masked by increases in others, particularly in those close to the target value of Hb A_{1c} of $< 7.0\%$ (37).

In the study by Bubner et al., the investigators used noninferiority analyses and reported a difference in the percentage of patients with final Hb A_{1c} in target range of 9.3% (90% CI 2.9%–15.7%) based on imputed data. According to the raw data, the difference was 7.1% (1.3%–12.8%); thus although the overall difference changed, the conclusions drawn were the same (Caroline Laurence and Lisa Yelland, personal communication, May 23, 2010).

Data on treatment intensification were reported for the trials of Grieve et al. (21), Cagliero et al. (22), Kennedy et al. (31), and Agus et al. (33), albeit using different study designs and outcome measures; the results are summarized in Table 4. It was not possible to pool the results from these studies because of the variation in the terms by which the intensification of treatment was reported.

PATIENT SATISFACTION

A similar diabetes satisfaction questionnaire was employed in 2 trials (32, 34). In the trial of Grieve et al. (21), 73% of the participants completed a questionnaire requesting them to score 9 aspects of care. The investigators found no significant difference between the overall clinic satisfaction ($P = 0.54$), although there was a significant difference in the score given for information provided by staff in the POCT cohort ($P = 0.004$). In the trial of Khunti et al., which was reported in a separate article (32), 84% of eligible participants completed a questionnaire requesting them to score 25 aspects of care. There was no statistically significant difference in the overall satisfaction rating ($P = 0.50$) between randomized groups, or in satisfaction with information about results ($P = 0.70$) and arrangements for phlebotomy ($P = 0.89$). The latter results may be explained by the fact, noted by Khunti et al. (30), that the results were not discussed with the patients at the time of their POCT analysis.

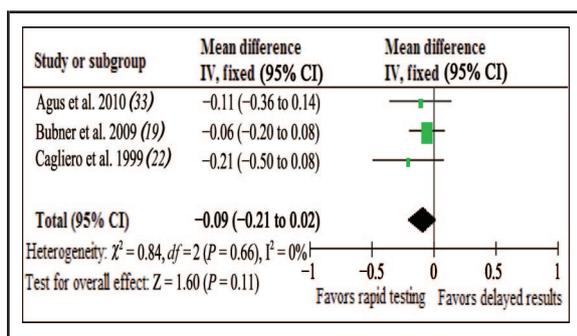


Fig. 1. Metaanalysis of results from trials in which the change in the mean Hb A_{1c} over the course of the trial was reported.

Table 3. Results from studies in which the change in the proportion of patients with an Hb A_{1c} ≤7.0% at the end of the trial was reported.

Trial	POCT Results				Delayed results			
	Baseline	End point			Baseline	End point		
		n <7%	Total n			n <7%	Total n	
Agus et al. (33)	18.9%	13.0%	10	77	23.1%	15.6%	10	64
Bubner et al. (19) ^a	56.1%	63.9%	537	840	45.8%	50.6%	315	622
Kennedy et al. (31), usual titration	0%	30%	409	1363	0%	32%	477	1491
Kennedy et al. (31), active titration	0%	41%	560	1366	0%	36%	540	1501
Khunti et al. (30)	44%	37%	107	290	37%	38%	117	309

^a Adjusted for clustering.

Laurence et al. (34) reported on a patient satisfaction study within the trial described by Bubner et al. (19), which included POCT for other parameters and conditions. They used a technique based on level of agreement with a number of statements and a mixed model analysis of variance. An overall response rate of 88% was reported and, overall, patients reported being satisfied with POCT. The POCT group reported a higher level of agreement than the control group with respect to the specimen collections process ($P < 0.001$) and confidence in the process ($P < 0.001$). They also reported that POCT strengthened their relationship with their primary care physician ($P < 0.010$) and enhanced their motivation for managing their own condition ($P < 0.001$).

COSTS AND USE OF HEALTH RESOURCES

A basic assessment of the use of resources was undertaken in 4 of the trials reported. Cagliero et al. (22) reported on the number of hypoglycemic episodes, the number of visits to the Emergency Department, letters

or telephone calls from doctors, and contact with nurses and found no difference between intervention and control cohorts. Grieve et al. (21) undertook an assessment of the cost per visit and the annual costs. The mean (SD) cost per visit was higher for the POCT, at £22.70 (£5.89) compared with the conventional approach at £14.00 (£6.05), but they found that using POCT reduced the mean (SD) number of visits to 1.81 (1.20) vs 2.28 (1.01), which meant there was a nonsignificant incremental cost saving for POCT (£31.92 vs £32.22). Khunti et al. (30) also found the mean annual diabetes-related cost per patient for the POCT group (£370.46) was slightly less than for usual care (£389.58). The mean costs of surgery [health center] contacts by the patients were lower (£72.00 for usual care vs £64.40 for POCT), as were the costs of contact with the hospital (£149.43 for usual care vs £111.60 for POCT). None of these differences was statistically significant.

Laurence et al. (35) undertook a more detailed cost-effectiveness analysis of the trial described by Bubner et al. (19). They calculated the costs of POCT and usual care for the tests, the direct costs to the health system, the direct costs to the patient, and the indirect (for time seeking healthcare) costs. The overall cost per patient was AUS\$3676 (95% CI \$3062–\$4191) for the POCT group compared to AUS\$3672 (95% CI \$2972–\$4628) for usual care.

Discussion

The results of this review of randomized trials suggests a modest and nonsignificant overall reduction in Hb A_{1c} of 0.09% between POCT and control groups. This finding does not provide evidence of the effectiveness of POCT for Hb A_{1c} in the management of diabetes. There are a number of limitations in the design of the trials included in this review that may have contributed to a failure to

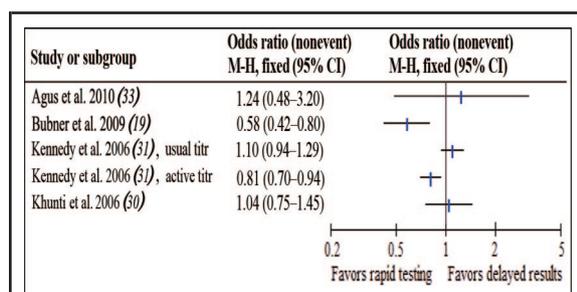


Fig. 2. Forest plot of results from trials in which the proportion of patients with an Hb A_{1c} ≤7.0% at the end of the trial was reported; M-H, Mantel–Haenszel test; titr, titration.

Table 4. Results from studies in which the proportion of patients in whom treatment was intensified over the course of the trial was reported.

Trial	Description of measure of intensification	POCT Results			Delayed results		
		n intensified	%	Total n	n intensified	%	Total n
Agus et al. (33)	Change in insulin dosing	47	61.0	77	39	61.1	64
Cagliero et al. (22)	Change in dose or frequency	59	68.6	86	65	83.3	78
Grieve et al. (21)	Management changes after receipt of Hb A _{1c} results	76	25.2	301	53	18.2	292
Kennedy et al. (31), (both trials)	Insulin dose at end point	Mean 55–56 IU (interquartile range 28–76 IU)			Mean 50 IU (interquartile range 24–66 IU)		

identify an intervention effect. Substantial variation between the studies in the proportion of patients considered within the target range ($\leq 7.0\%$) at baseline, as well as some of the studies including patients with type 1 or type 2 diabetes are likely to have limited the potential for reductions in Hb A_{1c} levels. Exploratory analyses within the trials might have provided additional data on impact for those with increased Hb A_{1c} levels (who might have benefited more from immediate knowledge, and discussion of the result, coupled with any change in therapy). In addition, the large variation in proportion of patients considered within target at the outset of the trial (0% to 56%) invalidated pooling of the data from the trials using this outcome measure, owing to the pooled statistic not necessarily reflecting the impact on those patients who might benefit from the immediate discussion of results. In regard to the impact of POCT on treatment intensification (a measure of the results being acted upon), the 2 studies excluded on the basis of their randomization protocol had greater intensification in patients with Hb A_{1c} levels $> 7.0\%$ (23, 27). Comparing the 2 trials reported by Kennedy et al. (31) in a population in which all participants had Hb A_{1c} levels $> 7.0\%$ at baseline, and in which the active titration was effectively treatment intensification compared with the usual care, active titration led to a higher proportion of patients in the POCT arm achieving Hb A_{1c} $\leq 7.0\%$ at the conclusion of the study, compared with POCT in the usual care arm [38% vs 30% ($P < 0.0001$)].

Although patient satisfaction appeared to improve with the use of POCT, there was no evidence that an improved relationship between patient and physician contributed to the improvement in the Hb A_{1c} in the Bubner et al. study (19). This again may represent a “floor effect” arising from the high proportion of patients with Hb A_{1c} $< 7.0\%$ at the commencement of the trial (56.1% in the POCT arm and 63.9% in the usual care arm).

A limitation of the current review is that a process of care including POCT for Hb A_{1c} was compared with the current standard of care, which in most instances was not

clearly defined, for example, in explaining how and when the most recent Hb A_{1c} results were communicated to, and discussed with, the patients. Discussion of the Hb A_{1c} level is a key element in discussions between patient and clinician about lifestyle and therapeutic management, and it has been shown that patients who are aware of their Hb A_{1c} level achieve better glycemic control (13). In 1 trial, however, the investigators did note that “it proved difficult for surgeries [health centers] to organize their management of patients with diabetes in such a way as to maximise the benefits of using the rapid test for intervention group patients. Practices therefore often continued their follow-up in the usual way.” The investigators also noted that “This also explains our failure to show any cost savings in terms of a reduction in appointments as the practices did not reorganise their clinics and the patients in many instances continued to attend twice” (30). A further limitation of the review in terms of definition of practice was related to the frequency of testing for Hb A_{1c}, although this could be deduced in 5 of the studies.

Bruns and Boyd have recently drawn attention to the impact of analytical performance of methods for measuring Hb A_{1c} (16) following the report of Leters-Westra et al. (15) that only 2 of 8 POCT systems for Hb A_{1c} met the performance criteria required for monitoring. Five of the studies reported in this review employed 1 of the systems reported as giving acceptable performance (15), although only 2 of the trials reported independent assessment of imprecision and bias as part of the trial. Kennedy et al. employed a system that was not National Glycohemoglobin Standardization Program certified at the time of the trials and expressed concern about the dispersion of Hb A_{1c} results when POCT results were compared with laboratory results, and the potential impact of interoperator variability, because there were more than 2000 operators involved in the trials (31, 36).

Results from 4 observational studies, in which there was immediate feedback of results and clinical decision making and more than 5700 patients were in-

volved, provide indirect support for the findings from randomized trials, all showing significant reductions in the Hb A_{1c} levels (21, 25, 38, 39). Thus Grieve et al. (21) undertook a retrospective cohort study of a sample of 1000 patients from a total of 1591 patients attending the diabetes clinics in 2 neighboring hospitals and showed a mean 7.79% (SE 0.058; 95% CI 7.67–7.90) in the POCT cohort, compared to a mean of 8.66% (SE 0.056; 95% CI 8.55–8.77) in the conventional care cohort ($P < 0.001$). Ferenczi et al. (25), in a retrospective review of medical records of new referrals following a change in practice, found that those patients receiving care with immediate Hb A_{1c} results showed a greater mean (SD) decrease in Hb A_{1c} [1.03% (0.33%)] compared to those for whom the result was communicated 2 days later [0.33% (0.83%)]. Petersen et al. (38) compared Hb A_{1c} levels retrospectively between 2 centers, over a 3-year period involving 4538 patients, 1 after the introduction of POCT for Hb A_{1c} measurement with immediate feedback of results, the other offering conventional care with delayed feedback of results. There was a decrease in the mean (SD) Hb A_{1c} from 7.75% (1.72%) to 7.35% (1.54%) ($P < 0.0001$) over the period of the study, with no significant change in the Hb A_{1c} results from the center offering conventional care. Finally Rust et al. (39), in a small before-and-after pilot study showed that POCT led to a significant reduction in Hb A_{1c} from 8.6% to 7.8% ($P = 0.004$) associated with therapeutic intensification.

Current service delivery models for diabetes management utilize Hb A_{1c} monitoring through a central laboratory service, with 1 of the following procedures: (a) a blood sample collected at the time of consultation, with subsequent feedback of results; (b) a self-collected finger-stick sample posted to the laboratory ahead of a clinic visit; (c) attendance at a phlebotomy center ahead of a clinic appointment, with results available at the consultation; or (d) a laboratory analyzer based in the hospital ambulatory clinic setting supported by a central laboratory service and operated by a laboratory technician. However, all of these approaches have practical limitations. For example, there can be a high failure rate of specimen receipt and suitability using a postal service (40), and outreach from a central laboratory has only limited applicability to the locality of a hospital service (21). Therefore, on-site POCT analyzers that can be maintained and used by clinical staff may have the potential to allow more productive discussions and motivate both clinician and patient to optimize management. However, such a change in practice would also involve significant process change and redistribution of resources e.g., with greater investment in the analytical element and disinvestment in repeat clinic time.

Evaluating POCT poses methodologic challenges because it is only 1 part of a complex intervention. Blinding clinicians and patients to the trial arm to which they are allocated is not possible, because a key element of the intervention is that a clinical decision is made at the time the result is produced; however, blinded measurement and reporting of outcomes is possible. This review has highlighted a number of additional issues that should be addressed in future studies. First, patients should be stratified according to baseline Hb A_{1c}, reflecting their potential to benefit from immediate feedback of Hb A_{1c} results. Second, POCT for Hb A_{1c} is a complex intervention involving not just the equipment but a change in the testing-consultation linkage, and in particular the need to ensure that the results are discussed with the patient at the same visit. It would be important to identify the process of current practice and define a clear process of care when employing POCT. Third, it is important to demonstrate that the POCT modality demonstrated the required level of analytical performance.

The conclusions from this review are that (a) there is currently insufficient evidence of the effectiveness of POCT for Hb A_{1c}; (b) the current research literature that addresses evaluation the role of POCT Hb A_{1c} requires further development, but provides support for further trials assessing the impact of evaluation in the context of active treatment changes; and (c) greater consideration should be given in future studies to (i) stratification of patients according to baseline Hb A_{1c}; (ii) clear definition of current process of care, as well as revised process of care using POCT; (iii) ensuring that results of POCT are discussed with patients when generated and that treatment decisions are documented and implemented; and (iv) ensuring that analytical performance of the POCT system meets quality specifications defined for monitoring utility. Audit of the use of POCT for the measurement of Hb A_{1c} as an integral part of an active diabetes program with close patient involvement over a longer period, such as that reported by Petersen et al. (38).

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