Title:  Clinical- and cost-effectiveness of the DCA 2000™ point of care testing device in diabetics

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Context And Policy Issues:

Diabetes is a chronic blood glucose regulation disorder that can lead to serious adverse effects such as heart disease, stroke, blindness, neuropathy, kidney disease, amputation, erectile dysfunction, and premature mortality.\(^1,2\) It is generally sub-divided into two categories: type 1 and 2. Type 1 diabetics have substantially reduced insulin secretion while type 2 diabetics have both a decreased secretion of and resistance to insulin. The end result is glucose remaining in the blood instead of being transported into cells to supply the body with the fuel it needs.\(^1\) More than 2 million Canadians have diabetes of whom 90% have type 2. The number of Canadians with type 2 diabetes is increasing due to a number of factors such as aging of the Canadian population, rising obesity rates, increasingly sedentary lifestyles, and the influx of high risk immigrants. Diabetes and its complications cost the Canadian healthcare system an estimated $13.2 billion every year.\(^2\)

Since poorly controlled blood glucose levels increase the risk of the aforementioned adverse effects,\(^1,3\) monitoring blood glucose levels is an important component of diabetes management. The standard for monitoring blood glucose control in diabetics is glycated haemoglobin (HbA1c) testing.\(^1,4\) HbA1c forms when glucose irreversibly attaches to the haemoglobin of red blood cells. Since red blood cells have a half-life of 60 to 90 days, the level of HbA1c reflects blood glucose levels over the past 2 to 3 months with the normal range for HbA1c levels being 4% to 6% of total haemoglobin.\(^1\) As microalbuminuria is the earliest indicator of renal disease attributable to diabetes, it is also monitored. Microalbuminuria relates to a range of albumin levels in urine, which although low, are above normal. Longitudinal research has shown microalbuminuria to be predictive of total mortality, cardiovascular mortality, and cardiovascular morbidity.\(^5\)

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Traditionally, HbA1c and microalbuminuria testing required laboratory analysis, but point of care testing (POCT) devices, such as Bayer’s DCA 2000™, presently allow office- or home-based testing with timely results. The DCA 2000™ measures HbA1c from a large drop of capillary blood (1 uL), and albumin, creatinine and the albumin to creatinine ratio from a small random sample of urine (40 uL).\(^1\)\(^,\)\(^6\) The DCA 2000™’s HbA1c test is certified by the National Glycohemoglobin Standardization Program which means its accuracy and precision has been tested and it is traceable to the Diabetes Control and Complications Trial (DCCT) reference method.\(^1\)\(^,\)\(^4\) Hence, HbA1c measurements obtained with the DCA 2000™ can be related to published long-term vascular risk findings documented by the DCCT and the United Kingdom Prospective Diabetes Study.\(^3\) The albumin to creatinine ratio produced by the DCA 2000™ has been verified in community and laboratory settings, and the first morning urine is recommended as the specimen of choice due to its greater sensitivity, specificity, and precision relative to a random spot urine.\(^7\) Finally, blood and urine test results are available in 6 and 7 minutes, respectively, reinforcing the timeliness of the results.\(^8\) Notwithstanding these advantages, the DCA 2000™ should not be used to screen for or diagnose diabetes or monitor day to day blood glucose control.\(^1\)

Point of care testing could provide greater convenience to patients, by condensing activities within one visit instead of multiple visits, and could allow for more informed, timely clinical decisions by healthcare providers. The expected overall impact would be improved therapeutic outcomes and reduced health costs. To evaluate this hypothesis, the empirical evidence regarding the clinical- and cost-effectiveness of the DCA 2000™ POCT device in diabetes patients was critically reviewed.

**Research Questions:**

1) What is the clinical-effectiveness of the DCA 2000™ POCT device in diabetics?
2) What is the cost-effectiveness of the DCA 2000™ POCT device in diabetics?

**Methods:**

A limited literature search was conducted on key health technology assessment resources, including PubMed, EMBASE, The Cochrane Library (Issue 3, 2007), University of York Centre for Reviews and Dissemination (CRD) databases, ECRI’s HTAIS, EuroScan, international HTA agencies, and a focused Internet search. Results include articles published between 1997 and the present, and are limited to English language publications only.

**Summary Of Findings:**

No health technology assessments, systematic reviews or meta-analyses were identified.

**Guidelines**

Guidelines produced by the Canadian Diabetes Association\(^8\) and National Institute for Clinical Excellence (NICE)\(^3\)\(^,\)\(^5\)\(^,\)\(^9\) as well as one position statement produced by the American Diabetes Association (ADA)\(^4\) were identified. The guidance provided by these organizations relates to testing frequency and therapeutic goals for HbA1c, albumin, and albumin to creatinine ratio rather than the specific use of the DCA 2000™ or other POCT devices. Notwithstanding this, NICE did recommend that HbA1c measurements be available during patient visits to allow immediate changes in insulin therapy and/or diet and thus reduce the need for follow-up appointments. However, this recommendation was based on less rigorous scientific evidence, such as that derived from expert committee reports or opinion, and/or clinical experience of respected authorities.\(^9\)
Randomized Controlled Trials

Two randomized controlled trials\textsuperscript{10,11} were identified. Khunti et al.\textsuperscript{10} examined the impact of HbA1c POCT using the DCA 2000™ on patients with Type 2 diabetes in a primary care environment. Eight practices were purposefully selected from 20 volunteering practices in order to ensure representation from rural and urban as well as deprived and affluent areas. Randomization occurred at the patient not practice level (n=319 per group, mean age=65.7 years). Practices were not required to make any organizational changes as the intervention was limited to use of the DCA 2000™ in place of traditional laboratory HbA1c testing. Exclusion criteria included patients who were unable to attend the practice and any who were exclusively under hospital care. At baseline, 44% (95% confidence interval (CI): 39%, 49%) and 37% (95% CI: 32%, 42%) of intervention and control patients, respectively, demonstrated good metabolic control (HbA1c<7%). At 12 months follow-up, the percentages were 37% (95% CI: 32%, 42%) and 38% (95% CI: 33%, 43%), respectively. A multiple logistic regression analysis which included baseline glycaemic control, sex, general practice attended, and duration of diabetes treatment at baseline indicated no statistically significant difference in the odds of good metabolic control in the intervention group relative to the control group after 12 months of follow-up (Odds Ratio=0.84, 95% CI: 0.58, 1.22). With respect to costs of diabetes related care, the mean cost per patient, from the perspective of the healthcare payer, did not significantly differ between the intervention (£370.46) and control (£389.58) groups over the 12 month period. Similarly, when considering patient-borne costs, no significant differences in mean costs were noted between intervention (£50.31) and control (£52.47) groups. The authors concluded that a rapid test to measure HbA1c in type 2 diabetics seen in primary care is unlikely to independently improve metabolic control or decrease costs. Study limitations included selecting practices from those volunteering to participate; a lack of blinding of the healthcare professionals and chart reviewer; the lack of additional measures to ensure optimal integration of POCT; and the conflict of interest created through equipment provision by Bayer Diagnostics.

Cagliero et al.\textsuperscript{11} examined the effect of HbA1c POCT in patients with type 1 and insulin treated type 2 diabetes attending a general hospital diabetes centre. Inclusion criteria included age older than 18 years; type 1 or insulin-treated type 2 diabetes for more than 1 year; care provided by the diabetes centre; and knowledge of English. Consecutive patients were randomly assigned to the intervention group (n=100, mean age=49 years), which had DCA 2000™ HbA1c levels determined at the time of the visit, or control group (n=101, mean age=49 years) which had HbA1c levels measured by the laboratory as per usual clinical practice. Relative to baseline, the intervention group demonstrated a statistically significant mean decrease in HbA1c at 6 months (mean decrease (sd)=0.57 (1.44)%, p=0.001) and 12 months follow-up (0.40 (1.65)%, p=0.013, conflicting standard deviation estimates in abstract and text with the more reasonable abstract estimate reported). Conversely, the control group did not demonstrate a significant decline at 6 months (0.11 (0.79)%, p>0.05) or 12 months follow-up (0.19 (1.16%), p>0.05). Statistically significant between group differences in the mean decrease in HbA1c were noted at 6 (p=0.029) but not 12 months (p=0.346). Mean daily insulin dose significantly increased over the 12 month period in the control (55.3 U/day to 59.9 U/day, p=0.012) but not intervention group (49.9 U/day to 50.7 U/day, p>0.05). Mean number of daily insulin injections did not significantly change in the control group (2.42 to 2.45, p>0.05) but significantly increased in the intervention group (2.29 to 2.45, p=0.001). There were no statistically significant differences in the proportion of patients reporting at least one severe hypoglycaemic event (intervention vs control: 30% vs 29%, p=0.917), the proportion of patients reporting at least one emergency room visit (15% vs 14%, p=0.464), or in the mean number of visits to the diabetes centre per year (4.72 vs 4.98, p>0.05). Finally, there was no significant difference in the mean number of healthcare related contacts by phone or letter between office visits (intervention vs control: 2.44 vs 2.73, p=0.239). The authors concluded that the immediate feedback of HbA1c
Observational Studies

Three observational studies were identified. Two specifically used the DCA 2000™ to provide POCT\textsuperscript{12,13} while the third used a Boehringer Mannheim turbidimetric immuno-inhibition assay.\textsuperscript{14} Miller et al.\textsuperscript{12} used a prospective controlled trial in a neighbourhood health centre to determine whether HbA1c test availability at the time of visit would increase the frequency of intensification of therapy and improve HbA1c levels at follow-up in patients with type 2 diabetes of at least 6 months duration. The clinic was staffed by 3 family practitioners, two general internists, and three nurse practitioners. During each visit, all patients had their HbA1c level measured with the DCA 2000™. If the baseline visit occurred on an even day of the month, HbA1c results were made available during the visit (n=317, mean age=61.0 years). Otherwise, HbA1c results were provided after the patient had left the clinic as per usual care (n=280, mean age=61.0 years). Among those patients with a baseline HbA1c of 7% or greater, the proportion experiencing an intensification of therapy at their baseline visit, defined as an increase in dosage of hypoglycaemic agents or the addition of a new agent, was significantly greater in the intervention group relative to the control group (51% vs 32%, p=0.0003). In these same patients, multiple logistic regression indicated that the odds of therapy intensification were 1.98 times greater (95% CI: 1.06, 3.71) in the intervention group after adjusting for baseline HbA1c, age, race, sex, duration of diabetes, body mass index, and glucose levels. At the first follow-up visit (mean time between visits=108 days), mean HbA1c levels did not significantly decline in either the intervention (8.5% to 8.3%, p=0.13, n=229) or control group (8.2% to 8.1%, p=0.56, n=211). At the second follow-up visit (mean time between visits=90 days), mean HbA1c levels significantly declined in the intervention (8.4% to 8.1%, p=0.04, n=141) but not control (8.1% to 8.0%, p=0.31, n=134) group. The authors theorized that the limited impact of the intervention on HbA1c levels might be due to the low frequency of intensification of therapy and possibly the use of increments of medications that were too low. They concluded that reductions in HbA1c levels may be modest unless technological innovation is accompanied by measures to help ensure that primary care providers take full advantage of the added information. Study limitations included the non-randomized assignment; the lack of blinding; the large proportion of African Americans which may limit generalizability to other ethnic groups; the loss to follow-up over time with only 74% and 46% having one and two follow-up visits, respectively, and those lost being significantly younger, having significantly lower random blood glucose, and significantly higher baseline HbA1c levels; and the conflict of interest created by loaning study equipment from Bayer.

Thaler et al.\textsuperscript{14} used a prospective controlled trial to examine the impact of HbA1c results availability on clinical decision making and subsequent diabetes control in patients with type 2 diabetes residing in an economically disadvantaged urban area and attending an outpatient specialty diabetes clinic. The usual clinic protocol was to advance therapy if fasting plasma glucose was 7.8 mmol/L or greater, or random plasma glucose was 10.0 mmol/L or greater. Therapy changes initially focused on diet and subsequently on initiation or intensification of pharmacological therapy to achieve a HbA1c level of 7.0% or less. In the trial, patients were assigned to have HbA1c results immediately available to their providers (n=575, mean age=58 years) or available to the provider after the patient visit (n=563, mean age=58 years). All patients had their fasting or random plasma glucose available during the patient visit as per pre-
intervention. With respect to outcomes, management was considered appropriate if patients with HbA1c values greater than 7% had their therapy intensified or patients with HbA1c values of 7% or less did not have their therapy intensified. The percentage of patients appropriately treated at their visit was significantly greater in the intervention group (79% vs 71%, p=0.03). Subgroup analysis revealed that the between group differences were primarily the result of less intensification of therapy in the intervention group relative to the control group when examining those patients with a baseline HbA1c of 7% or less (percentage with intensified therapy 10% vs 22%, p<0.0001). Multiple logistic regression indicated that providers were significantly more likely to intensify therapy for patients with higher fasting glucose and HbA1c levels and for patients treated with insulin or oral agents, irrespective of HbA1c availability (specific regression coefficients and p-values not provided). However, subgroup multiple logistic regression indicated that HbA1c availability significantly decreased the odds of therapy intensification in patients with a baseline HbA1c of 7% or less. For those patients returning for follow-up 2 to 7 months after their baseline visit, mean HbA1c levels significantly increased in both the intervention (7.5% to 7.9%, p=0.0005, n=278) and control groups (7.2% to 8.0%, p<0.0001, n=296), but a repeated measures ANOVA indicated the increase was significantly greater in the control group (p=0.02). In the subgroup with a baseline HbA1c level greater than 7%, a repeated measures ANOVA indicated that the intervention contributed significantly to a reduction of HbA1c at follow-up irrespective of whether the therapy was intensified or not. This lead the authors to suspect that the positive impact of immediate HbA1c levels may extend beyond appropriate adjustment of treatment. They theorized that greater provider confidence in the true state of glycaemic control led to more persuasive discussions during patient encounters and thus greater compliance with diet, exercise, and medications. Study limitations included the non-randomized assignment; the lack of blinding; the lack of measures of compliance with diet, exercise, or medications; the lack of details regarding recruitment and participation rates; incomplete follow-up data on HbA1c levels; and the relatively short period of follow-up.

Finally, using a prospective controlled trial, Grieve et al. examined the impact of a nurse POCT program piloted in a hospital practicing conventional care. Over a 3 month duration, patients attending routine hospital-based diabetes clinics were alternately assigned to intervention (n=302, mean age=59.7 years) or usual care groups (n=297, mean age=59.4 years). In the intervention group, physicians were supplied with blood glucose, DCA 2000™ HbA1c, lipids, and creatinine levels prior to the patient’s consultation. In the usual care group, blood glucose results were made available at the time of consultation and physicians had the option of requesting additional test(s), the results of which were generally provided several days after the patient consultation. Changes in care were ascertained by monitoring letters from the clinic physicians to the patients’ general practitioners. With respect to management changes related to glycaemic control, a statistically significant greater proportion of intervention patients were prescribed changes (25% vs 18%, p<0.05). Sub-group analyses revealed no significant differences between groups for patients with HbA1c levels less than 7.5% (10% vs 10%, p>0.05). However, for patients with HbA1c levels of 7.5% or greater, a statistically significant greater proportion of intervention patients underwent management changes relative to control patients (32% vs 21%, p<0.05). The mean cost per clinic visit, from the healthcare funder perspective, was significantly greater for the intervention group relative to usual care due to the higher number of tests processed and the higher capital equipment costs (£26.60 vs £14.00, p<0.05). Limiting POCT to HbA1c decreased the mean cost per visit to £17.91. A self-administered questionnaire completed by 280 patients indicated the intervention group was significantly more satisfied with their test information compared to the control group (p<0.001, no other details presented). After nurse POCT was introduced, semi-structured interviews were conducted with 10 clinic physicians. The clinicians stated that POCT improved clinical decision making and made them more confident about their decisions. Six out of 10 physicians stated they would not have to call patients back to the clinic so frequently and that availability of test
results helped with patient education. Physicians felt that lipid and creatinine testing was not as important as HbA1c testing. Grieve et al. concluded that POCT lead to more management changes in patients with poor glycaemic control and that clinical resistance would not be an obstacle to POCT implementation. Study limitations included non-randomized assignment; lack of blinding; confounding due to provision of lipids and creatinine results; examining the impact of POCT on the process of care rather than the outcomes of care which require longer durations of follow-up; the low participation rate for the self-administered questionnaire; and the conflict of interest resulting from a manufacturer loaning the study equipment.

Conclusions And Implications For Decision Or Policy Making:

Diabetes mellitus is a chronic, costly disease which is increasing in prevalence. If uncontrolled, it can lead to substantial adverse health effects. Since poorly controlled blood glucose levels increase the risk of adverse effects, monitoring blood glucose levels with HbA1c testing is probably the most important component of diabetes management. Guidelines are very consistent with respect to therapeudic targets and frequency of testing and NICE guidelines repeatedly reinforce the importance of availability of recent test results during patient consultations. Although traditionally a laboratory-based process, POCT devices, such as the Bayer DCA 2000™, provide accurate and timely results for HbA1c levels and albumin to creatinine ratios. Theoretically, the provision of these test results at the time of the patient’s visit would allow for more informed decision making and a consequent improvement in health outcomes and reduced health costs. In this review, no research was identified concerning POCT in paediatric populations and neither randomized controlled trials or observational studies have demonstrated consistently substantial clinical or cost benefits in the treatment of adult diabetics. Nonetheless, study limitations such as lack of organizational changes to ensure optimal integration of POCT, lack of clinical outcome measures, insufficient examination of higher risk subgroups, insufficient duration of follow-up and loss to follow-up impede definitive conclusions. With respect to outcomes requiring greater research, Thaler et al. reinforced the importance of measuring compliance with diet, exercise, and medications. They suggested that greater provider confidence in the true state of glycaemic control may lead to more persuasive discussions during patient encounters and thus greater compliance with treatment. Only Cagliero et al. examined hypoglycaemic events. Considering NICE’s emphasis on the importance of minimizing hypoglycaemic episodes, this outcome should probably be monitored in future studies.

Obviously, well-conducted randomized controlled trials which address the previously detailed limitations are needed. To minimize the issues of blinding and control group contamination, future trials should randomize practices rather than patients to intervention and control groups. Such an approach would also allow more effective implementation of the organizational changes needed to ensure the POCT device is optimally integrated.

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References:

1. Office-based point-of-care testing (POCT) for immediate feedback of hemoglobin A1c (HbA1c) [database online]. In: Target Database. Plymouth Meeting (PA): ECRI; 2002.


