Journal of Diabetes Science and Technology
Volume 6, Issue 2, March 2012

TECHNOLOGY REPORT

Accuracy and Precision of the Axis-Shield Afinion Hemoglobin A1c Measurement Device

Jamie R. Wood, M.D.,[1] Brett M. Kaminski, B.S.,[2] Craig Kollman, Ph.D.,[2] Roy W. Beck, M.D., Ph.D.,[2] Callyn A. Hall, B.S.,[2] Jason P. Yun, B.A.,[1] Eda Cengiz, M.D.,[3] Michael J. Haller M.D., M.S.C.I.,[4] Krishna Hassan, M.D.,[5] Georgeanna J. Klingensmith, M.D.,[6] and William V. Tamborlane, M.D.[3]

Abstract

Background:

The Afinion HbA1c (Axis-Shield) is a newer point-of-care device for measurement of hemoglobin A1c (A1C) using a boronate affinity method unlike the more commonly used DCA immunoassay method (Siemens Medical Solutions Diagnostics). The Afinion's accuracy and precision, when compared with high-performance liquid chromatography (HPLC) and DCA methods, have not been established in pediatric practice settings.

Methods:

Capillary blood was collected from 700 subjects with diabetes mellitus at seven Pediatric Diabetes Consortium sites. Each subject's A1C was measured locally using Afinion and DCA devices, and by a central laboratory (University of Minnesota) using a Tosoh HPLC method. In addition, repeated measurements on six whole blood samples provided by the National Glycohemoglobin Standardization Program (NGSP) were taken at three clinical centers using the Afinion and DCA methods and centrally using the Tosoh HPLC method to assess the precision of each device.

Results:

The coefficient of variation for measurements of whole blood samples for precision analysis was 2% for Afinion, 3% for DCA, and 1% for HPLC. In the patient samples measured at the seven clinic sites, the Afinion generated higher A1C results than the HPLC (mean difference = +0.15; $p < 0.001$), while the DCA produced lower values (mean difference = −0.19; $p < 0.001$). The absolute differences with HPLC were similar for the Afinion and DCA (median 0.2%) with a slight advantage for the Afinion when compared with DCA ($p < 0.001$ by rank test). The DCA tended to read lower than HPLC, particularly at high A1C levels ($p < 0.001$), while the Afinion's accuracy did not vary by A1C.

continued →

Author Affiliations: [1]Children's Hospital Los Angeles, Los Angeles, California; [2]Jaeb Center for Health Research, Tampa, Florida; [3]Yale School of Medicine, New Haven, Connecticut; [4]University of Florida, Gainesville, Florida; [5]Baylor College of Medicine, Houston, Texas; and [6]Barbara Davis Center for Childhood Diabetes, Aurora, Colorado

Abbreviations: (A1C) hemoglobin A1c, (CI) confidence interval, (CV) coefficient of variation, (DirecNet) Diabetes Research in Children Network, (HPLC) high-performance liquid chromatography, (NGSP) National Glycohemoglobin Standardization Program, (PDC) Pediatric Diabetes Consortium, (POC) point of care, (RAD) relative absolute difference, (SD) standard deviation

Keywords: accuracy, diabetes mellitus, glycated hemoglobin, HbA1c, point-of-care testing, precision

Corresponding Author: Jamie R. Wood, M.D., Jaeb Center for Health Research, 15310 Amberly Drive, Suite 350, Tampa, FL 33647; email address pdc@jaeb.org

Abstract cont.

Conclusions:

When compared to the central laboratory HPLC method, the differences between the results of the Afinion and DCA devices are clinically insignificant, and the Afinion and DCA have similar accuracy and precision when used in pediatric practice settings.

J Diabetes Sci Technol 2012;6(2):380-386

Introduction

Since 2000, point-of-care (POC) hemoglobin A1c (A1C) measurements have become part of standard practice in the management of individuals with diabetes. Point-of-care A1C results allow diabetes care providers to give patients immediate feedback and make timely decisions regarding optimal treatment regimens. As such, POC A1C testing has been associated with improvements in glycemic control.[1,2]

DCA devices are the most commonly used POC A1C devices and utilize a monoclonal antibody agglutination reaction to provide results in approximately 6 min. This method specifically recognizes the glycated N-terminus of the beta chain of the hemoglobin molecule. Importantly, the Diabetes Research in Children Network (DirecNet) demonstrated that DCA results generated in pediatric practice settings compared favorably with those obtained using the high-performance liquid chromatography (HPLC) method at the DCCT/EDIC Central Laboratory at the University of Minnesota.[3] The Afinion POC device was released in 2005 and employs a boronate affinity method and provides results in 3 min. In contrast to the DCA, the boronate affinity method detects attachment of glucose at non-N-terminal sites and N-terminal sites of the beta chain of the hemoglobin molecule. The resulting higher A1C signal is adjusted through internal correction equations prior to the device reporting a result. Both devices are Clinical Laboratory Improvement Amendments-waived and National Glycohemoglobin Standardization Program (NGSP) certified. The different methodologies used in the two devices also result in significant differences in potential interfering substances (hemoglobin variants, carbamylated hemoglobin).

Unlike the DCA,[3] the accuracy and precision of the Afinion has not been established in pediatric practice settings. Therefore, the aim of this study was to compare the accuracy and precision of the Axis-Shield Afinion A1C POC device with a HPLC A1C measurement by a central laboratory and to compare the accuracy with that of the DCA when measured in the clinical practice setting of seven Pediatric Diabetes Consortium (PDC) centers.[4]

Methods

Patient Samples for Accuracy Analyses

Research subjects were eligible to participate in the study if they had a clinical diagnosis of diabetes and were receiving diabetes care at one of seven clinical centers in the PDC. The study enrolled 100 subjects at each of the seven centers for a total of 700 research participants. Written or verbal informed consent was obtained as determined by the Institutional Review Board at each clinical center.

Each subject had three capillary blood samples collected from a finger prick using a sterile lancet device after the finger was cleaned with an alcohol swab. The A1C level was measured at the clinical center for two samples: one with the DCA (DCA 2000 at one center and DCA Vantage at six centers) and the other with the Afinion. Samples were collected and processed according to the user manuals of the two devices to reflect performance in typical clinical practice. All sites used Afinion reagents from the same lot that was currently being distributed on the market at the time of the study. Each site used their own supply of DCA cartridges. To assess accuracy of the POC devices, the third capillary blood sample was sent to the central laboratory at the University of Minnesota Medical Center, which was used in the DirecNet study.[3] The central laboratory measured A1C by the HPLC method (Tosoh HPLC Glycohemoglobin Analyzer, Tosoh Medics, Inc., San Francisco, CA).

National Glycohemoglobin Standardization Program Whole Blood Samples for Precision Analyses

To compare the precision of the DCA and Afinion with the HPLC method in the central laboratory, three clinical centers (Stanford, Colorado, and Yale) and the central laboratory received a set of six whole blood samples with assigned values by the NGSP (two low, two medium, and two high). Each of these samples was run in duplicate every day for three consecutive days on the DCA Vantage/DCA 2000 and Afinion devices at each clinical center and by Tosoh HPLC method at the central laboratory.

Statistical Analysis

Precision analyses were conducted using the repeated A1C measurements of the six whole blood samples provided by NGSP. For each sample, the standard deviation (SD) was taken as the simple SD of the six repeated measurements. The combined value (pooled over the six samples) was defined as the root mean square value from a repeated measures regression model. Residual values were examined and confirmed to have an approximate normal distribution. Coefficient of variation (CV), which represents instrument variation as a percentage of the mean, was calculated as the within-sample SD divided by the mean A1C.

For assessing accuracy of patient samples, samples with an HPLC A1C greater than 13.5% ($n = 7$) were excluded from the analysis, since the A1C range is limited by the Afinion and DCA to an upper limit of 15% and 14%, respectively. Of the 693 remaining samples, 5 additional samples were excluded: 1 had an improper sample collection for the HPLC determination, 1 had an abnormal hemoglobin variant, and 3 had an undetermined A1C level from a device (2 with a low hemoglobin concentration and 1 with an A1C level exceeding the device's upper limit).

Accuracy analyses were performed for both Afinion and DCA devices using the HPLC A1C as the reference. For each subject, the difference (device value minus HPLC value), absolute value of difference, relative difference (difference divided by HPLC A1C), and relative absolute difference (RAD; absolute difference divided by HPLC A1C) were calculated for both the Afinion and DCA measurements. The 95% limits of agreement and Bland–Altman plots were constructed for each device. For each device, least squares regression was used to determine if the mean difference between the device and HPLC A1C varied by underlying A1C level (estimated by the average A1C of the device and HPLC). The variance of differences was examined for constancy across the underlying A1C using the method of Bland.[5] Because the variance was found to increase with higher A1C levels for both devices, limits of agreement were constructed for subgroups of A1C.

For each subject, the difference between the Afinion and DCA absolute value of the difference (|Afinion − HPLC| − |DCA − HPLC|) was evaluated using the Wilcoxon signed-rank test. The influence of HPLC A1C on the magnitude of the differences was examined using least squares regression, modeling each factor separately. The van der Waerden normal rank scores of the absolute value of the difference and of the continuous factors were used in the models because of the skewed distribution of the absolute value of the difference data.

All reported p values are two-sided. Because of multiple comparisons, only p values less than 0.01 were considered statistically significant. All analyses were conducted using SAS version 9.2 (SAS Institute, Cary, NC).

Results

Whole Blood Samples Provided by the National Glycohemoglobin Standardization Program for Precision Analyses

The within-sample SD of the repeated A1C measurements on the NGSP samples was 0.18% for Afinion, 0.23% for DCA, and 0.06% for the HPLC. The corresponding CV was 2% for Afinion, 3% for DCA, and 1% for the HPLC. Precision did not vary meaningfully across samples (**Table 1**) or by center (data not shown).

Patient Samples for Accuracy Analyses

Mean age (±SD) of the 688 subjects was 13.5 ± 5.0 years; 49% were female; 70% were white, 16% were Hispanic or Latino, 9% were African American, and 4% were Asian. Mean HPLC A1C was 8.4% ± 1.7%. Mean HPLC A1C ranged from 8.1% to 9.2% across the seven centers.

On average, the Afinion generated higher A1C results than the HPLC with a mean difference of +0.15 [95% confidence interval (CI): +0.12, +0.17; $p < 0.001$], while the DCA produced lower values with a mean difference of −0.19 (95% CI: −0.22, −0.17; $p < 0.001$). The absolute differences with HPLC were similar for the Afinion and DCA (median 0.2% for each device; 73% for Afinion vs 67% for the DCA were within ±0.3% of HPLC; **Table 2**), with a slight advantage for the Afinion when compared with DCA ($p < 0.001$ by rank test). DCA accuracy varied between centers with one

Table 1.
Precision Analysis of Repeated Measurements of Whole Blood Samples

Whole blood samples[a]	Mean A1C[b]	Afinion			DCA			HPLC		
		N	SD_{ws}[c]	CV[d] (%)	N	SD_{ws}[c]	CV[d] (%)	N	SD_{ws}[c]	CV[d] (%)
All samples	7.48	108	0.18	2	108	0.23	3	36	0.06	1
Sample A	5.60	18	0.15	3	18	0.19	3	6	0.00	0
Sample B	5.66	18	0.12	2	18	0.24	4	6	0.05	1
Sample C	6.61	18	0.15	2	18	0.11	2	6	0.04	1
Sample D	8.09	18	0.15	2	18	0.15	2	6	0.08	1
Sample E	9.46	18	0.26	3	18	0.24	3	6	0.05	1
Sample F	9.47	18	0.19	2	18	0.36	4	6	0.08	1

[a] Samples were provided by the NGSP.
[b] Mean A1C is the average of six repeated HPLC measurements per sample measured at the central laboratory at the University of Minnesota.
[c] Within-sample standard deviation (SD_{ws}) was estimated by repeated measures regression model.
[d] Coefficient of variation (CV) is SD_{ws} divided by mean A1C.

Table 2.
Accuracy Analysis of Subject Samples

Comparison measure	Afinion vs HPLC (*N* = 688)	DCA vs HPLC (*N* = 688)
Difference[a]		
Mean (SD)	+0.15 (0.31)	−0.19 (0.36)
Median	+0.1	−0.2
Percentiles		
5th	−0.4	−0.8
25th	0.0	−0.4
75th	+0.3	0.0
95th	+0.7	+0.3
Absolute difference[b]		
Mean (SD)	0.26 (0.22)	0.31 (0.27)
Median	0.2	0.2
Percentiles		
5th	0.0	0.0
25th	0.1	0.1
75th	0.4	0.4
95th	0.7	0.8
Percentage of differences		
Within ± 0.1%	37%	34%
Within ± 0.3%	73%	67%
Within ± 0.5%	92%	82%

[a] Difference = device (Afinion or DCA) minus HPLC A1C.
[b] Absolute value of the difference.

center having slightly better accuracy than the other six centers (**Table 3**). The percentage of DCA values within 0.3% of the HPLC was 91% at one center compared with a range of 55–71% at the other centers. Afinion accuracy also varied between centers with percentage of values within 0.3% of the HPLC at each center ranging from 65% to 84%.

The absolute difference of the Afinion and DCA devices compared with HPLC increased with higher HPLC A1C ($p = 0.008$ for Afinion, $p < 0.001$ for DCA; **Table 3**). The median RAD of DCA measurements increased from 1.7% for HPLC A1C values <7.0% to 4.4% for HPLC values ≥10.0%, while Afinion RAD was similar across the range of HPLC A1C (**Table 3**).

The Afinion mean difference did not vary meaningfully across A1C ($p = 0.86$; **Figures 1** and **2**). The 95% limits of agreement were −0.2 to +0.6 for A1C <8.0%, widened to −0.5 to +0.7 for A1C 8.0–<10.0%, and −0.7 to +1.1 for A1C ≥ 10%. Conversely, the DCA tended to read lower than the HPLC reference, particularly at high A1C levels ($p < 0.001$; **Figures 3** and **4**). The 95% limits of agreement were −0.6 to +0.4 for A1C <8.0%, −1.0 to +0.4 for A1C 8.0–<10.0%, and −1.4 to +0.8 for A1C ≥10.0%.

Discussion

Point-of-care measurement of A1C has become standard of care in many clinics managing patients with diabetes. As newer POC A1C devices become available, evaluation of performance in typical clinical settings, as well as comparison with reference standards and other commonly

Table 3.
Accuracy Compared with HPLC by A1C and Center

	N	Mean difference[a]		Mean relative difference[b]		Median absolute difference[c]		Median relative absolute difference[d]		Percentage within ± 0.3	
		Afinion	DCA	Afinion (%)	DCA (%)	Afinion	DCA	Afinion (%)	DCA (%)	Afinion (%)	DCA (%)
Overall	688	+0.15	−0.19	+1.9	−2.1	0.2	0.2	2.6	2.8	73	67
By HPLC A1C											
<7.0%	122	+0.24	−0.02	+3.9	−0.2	0.2	0.1	3.3	1.7	74	93
7.0–<8.0%	182	+0.18	−0.10	+2.4	−1.4	0.2	0.2	2.6	2.6	77	83
8.0–<9.0%	157	+0.08	−0.19	+1.0	−2.3	0.2	0.2	2.3	2.5	80	69
9.0–<10.0%	107	+0.05	−0.35	+0.5	−3.7	0.2	0.4	2.2	4.3	73	43
≥10.0%	120	+0.18	−0.37	+1.6	−3.3	0.3	0.5	2.9	4.4	54	35
By Center											
A	99	+0.17	−0.11	+2.1	−1.0	0.2	0.2	2.7	2.4	65	70
B	100	+0.12	−0.33	+1.5	−3.5	0.2	0.3	2.5	3.8	67	55
C	96	+0.12	−0.19	+1.8	−2.0	0.2	0.2	2.2	2.9	82	70
D	95	+0.15	−0.24	+1.7	−2.5	0.2	0.3	2.4	3.4	71	56
E	100	+0.19	+0.10	+2.5	+1.3	0.2	0.1	2.6	1.6	74	91
F	100	+0.27	−0.22	+3.3	−2.6	0.3	0.2	3.4	2.8	67	71
G	98	+0.01	−0.37	+0.5	−4.3	0.2	0.3	2.0	4.0	84	55

[a] Difference = Device (Afinion or DCA) minus HPLC A1C.
[b] Relative difference = Difference divided by HPLC A1C
[c] Absolute difference = Absolute value of the difference
[d] Relative absolute difference = Absolute difference divided by HPLC A1C

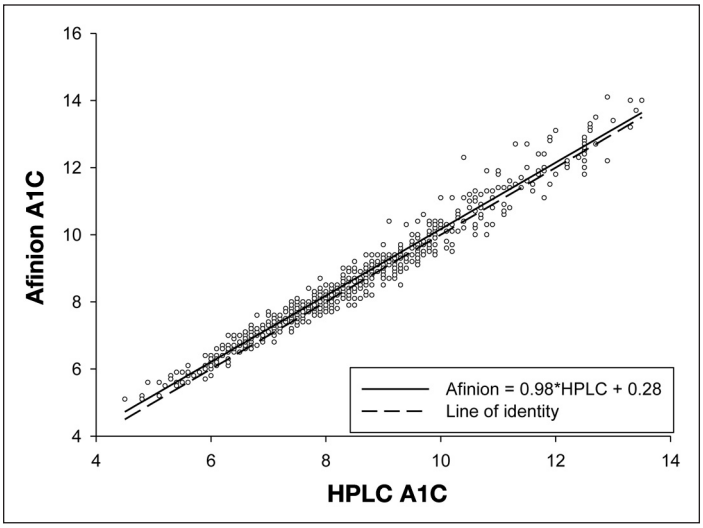

Figure 1. Afinion versus HPLC A1C measurements (*N* = 688).

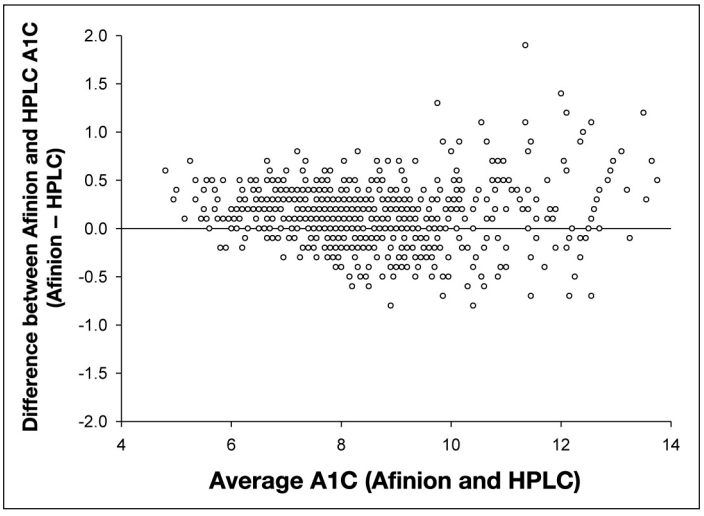

Figure 2. Bland–Altman plot of Afinion and HPLC A1C measurements (*N* = 688).

used A1C devices, are needed. In this study, we compared the accuracy and precision of the Afinion and DCA A1C devices with the Tosoh HPLC method in 688 individuals with diabetes receiving care at one of seven clinical centers of the PDC. The subjects are representative of pediatric patients with diabetes in the United States with an equal gender distribution, expected ethnic distribution, and wide spectrum of A1C levels.

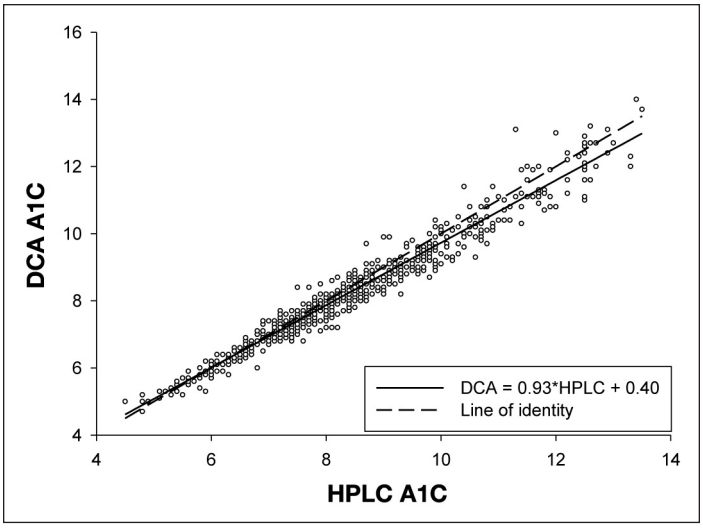

Figure 3. DCA versus HPLC A1C measurements (N = 688).

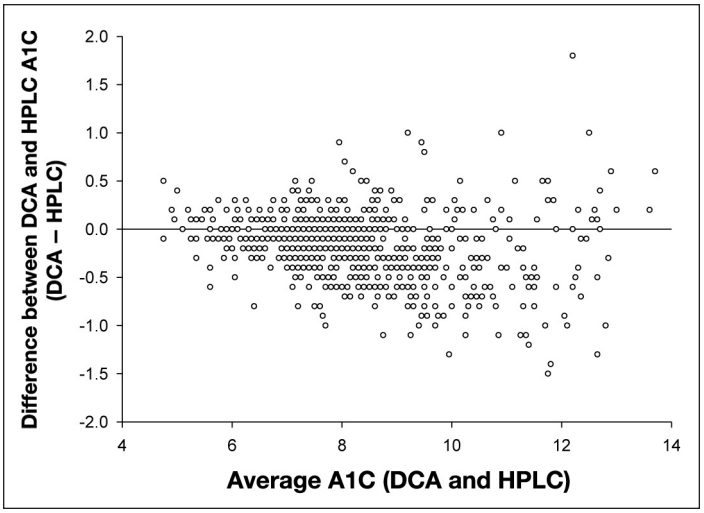

Figure 4. Bland–Altman plot of DCA and HPLC A1C measurements (N = 688).

The Afinion A1C device generated higher results than HPLC, while the DCA produced lower results than HPLC. The higher results that we observed with the Afinion compared to the DCA could be attributed to differences in methodology or calibration between the two devices. Both devices had similar absolute differences compared with HPLC, with the Afinion being slightly more accurate in comparison with the DCA. The Afinion was significantly more accurate and precise than the DCA when both were compared to HPLC, and this finding could be explained by the fact that a single reagent lot was used for the Afinion across sites in comparison to potentially more than one lot for the DCA reagents. Other groups have described significant lot-to-lot variability with POC reagents.[6] While these statistical differences are unlikely to be clinically meaningful, these data show that the accuracy of the Afinion A1C device is similar to the more commonly used DCA.

A review of the literature in this area reveals that the direction and magnitude of the bias for the Afinion and DCA device varies across studies. Some studies have demonstrated that the DCA produces lower A1C measurements,[7–10] while the Afinion produces higher A1C measurements[11] than HPLC comparison method used in each study. Two groups have reported higher results from DCA devices when compared with HPLC,[3,11] and two groups have reported lower results from the Afinion when compared with HPLC method in their samples.[6,10] The varied results could be explained by the fact that different studies used different HPLC methods with their own biases.

Notably, one DCA device in this study produced slightly higher results than HPLC (mean difference of +0.1) and had a higher percentage (92%) of values within ±0.3% of HPLC. Excluding this center, Afinion and DCA variability between centers was similar. The observed difference may be related to device recalibration methods and variance in cartridge lots.

The Afinion mean difference did not vary meaningfully across A1C, whereas we found that the DCA tended to read low particularly at higher A1C. Petersen and colleagues[10] also found that the DCA Vantage and the Afinion increasingly underestimated the A1C as HPLC A1C value increased. Although the clinician needs to take this into account when interpreting a POC A1C result, this finding is unlikely to have a large clinical impact given that management decisions based on an A1C in the very high range are likely to be the same.

The Afinion and DCA also had similar CV in our study when compared with the HPLC method (2%, 3%, and 1%, respectively). This result is consistent with those found in other studies, which have reported CV results ranging from 1.55% to 3.93% for DCA devices[6,7,9–11] and 0.5% to 2.66% for the Afinion.[6,10,11]

Conclusions

Although there are statistically significant differences in the performance of the Afinion and DCA A1C devices when compared with the reference standard, overall we found the differences to be clinically insignificant and conclude that the Afinion device is similar to the DCA device in both accuracy and precision. However, in the daily operation of busy diabetes clinics, the speed of the Afinion device may have advantages over the DCA.

Funding:

The Pediatric Diabetes Consortium and its activities are funded through an unrestrictive grant from Novo Nordisk through its Changing Diabetes® Leadership Initiative. The University of Michigan center was supported by the Michigan Diabetes Research and Training Center funded by DK020572 from the National Institute of Diabetes and Digestive and Kidney Diseases.

Acknowledgements:

The participating clinical centers are the Barbara Davis Center at the University of Colorado, Baylor College of Medicine, Children's Hospital of Los Angeles, Stanford University, University of Florida, University of Michigan, and Yale University. The Jaeb Center for Health Research is the coordinating center and the primary contractor of the unrestricted grant from Novo Nordisk, Inc. Axis-Shield provided Afinion HbA1c devices and cartridges to the PDC centers.

References:

1. Miller CD, Barnes CS, Phillips LS, Ziemer DC, Gallina DL, Cook CB, Maryman SD, El-Kebbi IM. Rapid A1C availability improves clinical decision-making in an urban primary care clinic. Diabetes Care. 2003;26(4):1158–63.
2. Petersen JR, Finley JB, Okorodudu AO, Mohammad AA, Grady JJ, Bajaj M. Effect of point-of-care on maintenance of glycemic control as measured by A1C. Diabetes Care. 2007;30(3):713–15.
3. Tamborlane WV, Kollman C, Steffes MW, Ruedy KJ, Dongyuan X, Beck RW, Chase P, Fox LA, Wilson DM, Tsalikian E; Diabetes Research in Children Network (DirecNet) Study Group. Comparison of fingerstick hemoglobin A1c levels assayed by DCA 2000 with the DCCT/EDIC central laboratory assay: results of a Diabetes Research in Children Network (DirecNet) Study. Pediatr Diabetes. 2005;6(1):13–16.
4. Pediatric Diabetes Consortium. The Pediatric Diabetes Consortium: improving care of children with type 1 diabetes through collaborative research. Diabetes Technol Ther. 2010;12(9):685–8.
5. Bland JM, Altman DG. Measuring agreement in method comparison studies. Stat Methods Med Res. 1999;8(2):135–60.
6. Lenters-Westra E, Slingerland RJ. Six of eight hemoglobin A1c point-of-care instruments do not meet the general accepted analytical performance criteria. Clin Chem. 2010;56(1):44–52.
7. Arsie MP, Marchioro L, Lapolla A, Giacchetto GF, Bordin MR, Rizzotti P, Fedele D. Evaluation of diagnostic reliability of DCA 2000 for rapid and simple monitoring of HbA1c. Acta Diabetol. 2000;37(1):1–7.
8. Guerci B for the DCA Study Group. Multicentre evaluation of the DCA 2000 system for measuring glycated haemoglobin. Diabetes Metab. 1997;23(3):195–201.
9. Szymezak J, Leroy N, Lavalard E, Gillery P. Evaluation of the DCA Vantage analyzer for HbA1c assay. Clin Chem Lab Med. 2008;46(8):1195–8.
10. Petersen JR, Omoruyi FO, Mohammad AA, Shea TJ, Okorodudu AO, Ju H. Hemoglobin A1c: assessment of three POC analyzers relative to a central laboratory method. Clin Chim Acta. 2010;411(23–24):2062–6.
11. Sanchez-Mora C, Rodriguez-Oliva MS, Fernandez-Riejos P, Mateo J, Polo-Padillo J, Goberna R, Sánchez-Margalet V. Evaluation of two HbA1c point-of-care analyzers. Clin Chem Lab Med. 2011;49(4):653–7.