Ontario
Health Quality Ontario
Qualité des services de santé Ontario

Point-of-Care Hemoglobin A_{1c} Testing: An Evidence-Based Analysis

Health Quality Ontario

July 2014

Ontario Health Technology Assessment Series; Vol. 14: No. 8, pp. 1–30, July 2014

Suggested Citation

This report should be cited as follows:

Health Quality Ontario. Point-of-care hemoglobin A_{1c} testing: an evidence-based analysis. Ont Health Technol Assess Ser [Internet]. 2014 July;14(8):1–30. Available from: http://www.hqontario.ca/evidence/publications-and-ohtac-recommendations/ontario-health-technology-assessment-series/eba-point-of-care-a1c

Permission Requests

All inquiries regarding permission to reproduce any content in the *Ontario Health Technology Assessment Series* should be directed to EvidenceInfo@hqontario.ca.

How to Obtain Issues in the *Ontario Health Technology Assessment Series*

All reports in the *Ontario Health Technology Assessment Series* are freely available in PDF format at the following URL: http://www.hqontario.ca/evidence/publications-and-ohtac-recommendations/ontario-health-technology-assessment-series.

Conflict of Interest Statement

The members of the Division of Evidence Development and Standards at Health Quality Ontario are impartial. There are no competing interests or conflicts of interest to declare.

Indexing

The *Ontario Health Technology Assessment Series* is currently indexed in MEDLINE/PubMed, Excerpta Medica/Embase, and the Centre for Reviews and Dissemination database.

Peer Review

All reports in the *Ontario Health Technology Assessment Series* are subject to external expert peer review. Additionally, Health Quality Ontario posts draft reports and recommendations on its website for public comment prior to publication. For more information, please visit: http://www.hqontario.ca/en/mas/ohtac_public_engage_overview.html.

About Health Quality Ontario

Health Quality Ontario is an arms-length agency of the Ontario government. It is a partner and leader in transforming Ontario's health care system so that it can deliver a better experience of care, better outcomes for Ontarians, and better value for money.

Health Quality Ontario strives to promote health care that is supported by the best available scientific evidence. The Evidence Development and Standards branch works with expert advisory panels, clinical experts, scientific collaborators, and field evaluation partners to conduct evidence-based reviews that evaluate the effectiveness and cost-effectiveness of health interventions in Ontario.

Based on the evidence provided by Evidence Development and Standards and its partners, the Ontario Health Technology Advisory Committee—a standing advisory subcommittee of the Health Quality Ontario Board—makes recommendations about the uptake, diffusion, distribution, or removal of health interventions to Ontario's Ministry of Health and Long-Term Care, clinicians, health system leaders, and policymakers.

Health Quality Ontario's research is published as part of the *Ontario Health Technology Assessment Series,* which is indexed in MEDLINE/PubMed, Excerpta Medica/Embase, and the Centre for Reviews and Dissemination database. Corresponding Ontario Health Technology Advisory Committee recommendations and other associated reports are also published on the Health Quality Ontario website. Visit http://www.hqontario.ca for more information.

About the *Ontario Health Technology Assessment Series*

To conduct its comprehensive analyses, Evidence Development and Standards and its research partners review the available scientific literature, making every effort to consider all relevant national and international research; collaborate with partners across relevant government branches; consult with expert advisory panels, clinical and other external experts, and developers of health technologies; and solicit any necessary supplemental information.

In addition, Evidence Development and Standards collects and analyzes information about how a health intervention fits within current practice and existing treatment alternatives. Details about the diffusion of the intervention into current health care practices in Ontario add an important dimension to the review.

The Ontario Health Technology Advisory Committee uses a unique decision determinants framework when making recommendations to the Health Quality Ontario Board. The framework takes into account clinical benefits, value for money, societal and ethical considerations, and the economic feasibility of the health care intervention in Ontario. Draft Ontario Health Technology Advisory Committee recommendations and evidence-based reviews are posted for 21 days on the Health Quality Ontario website, giving individuals and organizations an opportunity to provide comments prior to publication. For more information, please visit: http://www.hqontario.ca/evidence/evidence-process/evidence-review-process/professional-and-public-engagement-and-consultation.

Disclaimer

This report was prepared by the *Evidence Development and Standards branch* at Health Quality Ontario or one of its research partners for the *Ontario Health Technology Advisory Committee* and was developed from analysis, interpretation, and comparison of scientific research. It also incorporates, when available, Ontario data and information provided by experts and applicants to HQO. The analysis may not have captured every relevant publication and relevant scientific findings may have been reported since the development of this recommendation. This report may be superseded by an updated publication on the same topic. Please check the Health Quality Ontario website for a list of all publications: http://www.hqontario.ca/evidence/publications-and-ohtac-recommendations.

Abstract

Background

The increasing prevalence of diabetes in Ontario means that there will be growing demand for hemoglobin A_{1c} (HbA_{1c}) testing to monitor glycemic control for the management of this chronic disease. Testing HbA_{1c} where patients receive their diabetes care may improve system efficiency if the results from point-of-care HbA_{1c} testing are comparable to those from laboratory HbA_{1c} measurements.

Objectives

To review the correlation between point-of-care HbA_{1c} testing and laboratory HbA_{1c} measurement in patients with diabetes in clinical settings.

Data Sources

The literature search included studies published between January 2003 and June 2013. Search terms included glycohemoglobin, hemoglobin A_{1c}, point of care, and diabetes.

Review Methods

Studies were included if participants had diabetes; if they compared point-of-care HbA_{1c} devices (licensed by Health Canada and available in Canada) with laboratory HbA_{1c} measurement (reference method); if they performed point-of-care HbA_{1c} testing using capillary blood samples (finger pricks) and laboratory HbA_{1c} measurement using venous blood samples within 7 days; and if they reported a correlation coefficient between point-of-care HbA_{1c} and laboratory HbA_{1c} results.

Results

Three point-of-care HbA_{1c} devices were reviewed in this analysis: Bayer's A1cNow+, Bio-Rad's In2it, and Siemens' DCA Vantage. Five observational studies met the inclusion criteria. The pooled results showed a positive correlation between point-of-care HbA_{1c} testing and laboratory HbA_{1c} measurement (correlation coefficient, 0.967; 95% confidence interval, 0.960–0.973).

Limitations

Outcomes were limited to the correlation coefficient, as this was a commonly reported measure of analytical performance in the literature. Results should be interpreted with caution due to risk of bias related to selection of participants, reference standards, and the multiple steps involved in POC HbA_{1c} testing.

Conclusions

Moderate quality evidence showed a positive correlation between point-of-care HbA_{1c} testing and laboratory HbA_{1c} measurement. Five observational studies compared 3 point-of-care HbA_{1c} devices with laboratory HbA_{1c} assays, and all reported strong correlation between the 2 tests.

Plain Language Summary

Diabetes occurs when the body cannot use glucose normally. It happens because either the pancreas does not make enough insulin (a hormone that controls the level of glucose in the blood) or the body does not respond well to the insulin it makes. High blood glucose levels over a long time cause damage to the heart, eyes, kidneys, and nerves. Checking blood glucose levels often can help doctors choose the right treatment to help keep diabetes in control.

Hemoglobin A_{1c} (HbA_{1c}) is a test that measures the amount of glucose that has stuck to red blood cells over a 3-month period. It is directly related to a patient's average blood glucose levels. People with diabetes usually go to a laboratory to have their HbA_{1c} tested. However, testing HbA_{1c} in diabetes education centres or doctor's offices may save time and money. There is moderate quality evidence that testing HbA_{1c} where patients receive their diabetes care is comparable to measuring HbA_{1c} in a laboratory.

Table of Contents

List of Tables

List of Figures

List of Abbreviations

CI	Confidence interval
GRADE	Grading of Recommendations Assessment, Development, and Evaluation
HbA_{1c}	Hemoglobin A_{1c}
Lab HbA_{1c}	Laboratory hemoglobin A_{1c}
NGSP	National Glycohemoglobin Standardization Program
POC HbA_{1c}	Point-of-care hemoglobin A_{1c}
QUADAS	Quality Assessment of Diagnostic Accuracy Studies

Background

Overuse, underuse, and misuse of interventions are important concerns in health care and lead to individuals receiving unnecessary or inappropriate care. In April 2012, under the guidance of the Ontario Health Technology Advisory Committee's Appropriateness Working Group, Health Quality Ontario (HQO) launched its Appropriateness Initiative. The objective of this initiative is to develop a systematic framework for the ongoing identification, prioritization, and assessment of health interventions in Ontario for which there is possible misuse, overuse, or underuse.

For more information on HQO's Appropriateness Initiative, visit our website at www.hqontario.ca.

Objective of Analysis

The objective of this analysis was to review the correlation between point-of-care hemoglobin A_{1c} (POC HbA_{1c}) testing and laboratory hemoglobin A_{1c} (lab HbA_{1c}) measurement in patients with diabetes in clinical settings.

Clinical Need and Target Population

Description of Disease/Condition

Diabetes is a metabolic disorder resulting from defective insulin production and/or action. There are 2 major types of diabetes: type 1 and type 2. Type 1 diabetes is an autoimmune disease in which the body's defence system attacks its own insulin-producing cells; type 2 diabetes is characterized by insulin resistance and inadequate insulin production. Type 2 diabetes accounts for over 90% of the diabetes population. Left uncontrolled, the chronic hyperglycemia associated with diabetes contributes to cardiovascular disease and microvascular complications affecting the eyes, kidneys, and nerves. (1) Classic diabetes trials, including the Diabetes Control and Complications Trial for type 1 diabetes and the United Kingdom Prospective Diabetes Study for type 2 diabetes, have demonstrated that optimal glycemic control slows the onset and progression of diabetes-related complications. (2-4)

Hemoglobin A_{1c} (HbA_{1c}) is a marker of long-term glycemic control, and it has been widely used to guide treatment decisions in clinical practice. Its value reflects average blood glucose concentration over the preceding 3 months. (5) It is recommended that patients with diabetes have HbA_{1c} tested every 3 to 6 months to assess glycemic control. (6)

Ontario Prevalence

In 2012, Statistics Canada reported a prevalent diabetes population of 770,410 in Ontario. (7) This figure is expected to increase in parallel with the upward trend of obesity and the aging population.

Technology/Technique

Point-of-care testing refers to diagnostic testing at or near the site of patient care. (8) POC HbA_{1c} testing is an alternative to lab HbA_{1c} measurement, and it has several potential advantages. First, it provides rapid test results following blood collection, to expedite medical decision-making. Second, it may improve health system efficiency and be convenient for patients, because fewer visits to laboratories or physician's offices would be needed. Third, it may improve access to HbA_{1c} measurement for patients in underserved

populations (e.g., rural or remote communities).

POC HbA_{1c} requires a finger-prick blood sample. This capillary blood sample is applied to a reagent cartridge, which is then inserted into a desktop analyzer; HbA_{1c} is quantified and reported in 5 to 10 minutes. Point-of-care devices use different methods to measure HbA_{1c}, including boronate affinity chromatography and immunoassay. (9)

Similar to lab HbA_{1c} assays, POC HbA_{1c} devices must be certified by the United States National Glycohemoglobin Standardization Program (NGSP), and the results must be traceable to the Diabetes Control and Complications Trial Reference Method. (10) The certification process involves comparing the POC HbA_{1c} values of 40 patient samples with those from a Secondary Reference Laboratory. Currently, the bias criteria for 37 out of 40 results are within 7% of the NGSP Secondary Reference Laboratory findings, over an HbA_{1c} range of 4% to 10% (beginning in January 2014, the bias criteria will be tightened to within 6%). (11) Device certification is effective for 1 year, and is specific to the particular lot of reagent and the device used. (12) Point-of-care HbA_{1c} devices are waived under Clinical Laboratory Improvement Amendments (i.e., users are not required to participate in proficiency testing).

In 2010, Lenters-Westra et al (13) used the Clinical Laboratory Standard Institute protocols to evaluate the analytical performance of 8 POC HbA_{1c} devices in venous blood samples of patients with diabetes. They reported that at the time of writing, only 2 POC HbA_{1c} devices—DCA Vantage from Siemens and Afinion from Axis-Shield (not licensed by Health Canada)—met the criteria: that is, a coefficient of variation of < 3% and error criteria[1] of ± 0.85% as specified by the NGSP (in January 2010, the error criteria were lowered to ± 0.75%). (14) However, since experienced technologists at manufacturers' sites performed the certification under ideal conditions, the results of this study may not reflect the performance of these devices in clinical settings.

Ontario Context

The current standard of care in Ontario is that patients with diabetes go to community laboratories or hospitals for HbA_{1c} measurement, usually prior to their physician visit. POC HbA_{1c} devices are being used in selected diabetes education centres, community health centres, and doctor's offices, funded by their operating budgets.

The prevalence of POC HbA_{1c} testing in Ontario is unclear. However, considering the increasing prevalence of diabetes, there will be a growing need for HbA_{1c} testing to monitor glycemic control. POC HbA_{1c} testing may improve system efficiency if the results from point-of-care devices are comparable to those from laboratory assays. Therefore, Health Quality Ontario chose to compare the correlation between POC HbA_{1c} and lab HbA_{1c} measurement in clinical settings.

Regulatory Status

Six POC HbA_{1c} devices are licensed by Health Canada as class-3 devices for quantitative determination of HbA_{1c} from capillary or venous whole blood. The manufacturer information for these devices is presented in Table 1.

[1]95% confidence interval [CI] of the difference between POC HbA_{1c} and lab HbA_{1c} measurements.

Table 1: Manufacturer Information for POC HbA_{1c} Devices Licensed for Use in Canada

Manufacturer Information	A1c Now Self-Check at Home A_{1c} System	A1c Now+	DCA 2000 Analyzer System	DCA Vantage Analyzer	In2it (I) System	Smart Direct HbA1c Analyzer
Manufacturer	Bayer Healthcare LLC	Bayer Healthcare LLC	Siemens Healthcare Diagnostics Inc	Siemens Healthcare Diagnostics Inc	Bio-Rad Laboratories Deeside	Diazyme Laboratories
Licence number	84541	65484	1990	76034	80662	88752
Issue Date	November 2010	July 2008	March 1999	January 2008	September 2009	April 2012
Remark	—	—	Unavailable in Canada	—	—	Unavailable in Canada

Abbreviation: POC HbA_{1c}, point-of-care hemoglobin A_{1c}.

The operating characteristics of the 3 POC HbA_{1c} devices that are available for use in Canada are summarized in Table 2.

Table 2: Characteristics of POC HbA_{1c} Devices Available for Use in Canada

Characteristic	A1c Now+	DCA Vantage Analyzer	In2it (I) System
Manufacturer	Bayer Healthcare LLC	Siemens Healthcare Diagnostics Inc	Bio-Rad Laboratories Deeside
Method	Immunoassay	Latex agglutination inhibition immunoassay	Boronate-affinity chromatography
Blood sample	5 µL (capillary or venous)	1 µL (capillary or venous)	10 µL (capillary or venous)
Time for results	5 minutes	6 minutes	10 minutes
Interference with abnormal hemoglobin variants (15)	HbC, HbS, HbF > 10–15%	HbC, HbE, HbF > 10–15%	HbF > 10%
NGSP-certified (16)	Yes	Yes	Yes
CLIA waived	Yes	Yes	Yes
Other characteristics	Same device as A1c Now, with more test cartridges in the kit	Successor of DCA 2000	N/A

Abbreviation: CLIA, Clinical Laboratory Improvement Amendments; HbC, hemoglobin C; HbE, hemoglobin E; HbF, hemoglobin F; HbS, hemoglobin S; NGSP, National Glycohemoglobin Standardization Program; POC HbA_{1c}, point-of-care hemoglobin A_{1c}.

Evidence-Based Analysis

Research Question

What is the correlation between POC HbA_{1c} testing and lab HbA_{1c} measurements in patients with diabetes in clinical settings?

Research Methods

Literature Search

Search Strategy

A literature search was performed on June 17, 2013, using Ovid MEDLINE, Ovid MEDLINE In-Process and Other Non-Indexed Citations, Ovid Embase, EBSCO Cumulative Index to Nursing & Allied Health Literature (CINAHL), and EBM Reviews, for studies published from January 1, 2003, to June 17, 2013. (Appendix 1 provides details of the search strategies.) Abstracts were reviewed by a single reviewer and, for those studies meeting the eligibility criteria, full-text articles were obtained. Reference lists were also examined for any additional relevant studies not identified through the search.

Inclusion Criteria

- English-language full-text publications
- published between January 1, 2003, and June 17, 2013
- randomized controlled trials, observational studies, systematic reviews, and meta-analyses
- patients with type 1 or type 2 diabetes of all ages
- studies comparing POC HbA_{1c} devices (licensed by Health Canada and available on the Canadian market) with lab HbA_{1c} measurement (reference standard)
- POC HbA_{1c} testing with capillary blood samples from finger pricks and lab HbA_{1c} measurement with venous blood samples within 7 days

Exclusion Criteria

- studies that included participants without diabetes
- studies that used older generation of POC HbA_{1c} devices (e.g., DCA 2000 has been replaced by DCA Vantage, and is no longer on Canadian market)
- studies that used finger-prick capillary blood samples for both POC HbA_{1c} and lab HbA_{1c} measurements
- studies that used venous whole blood samples for both POC HbA_{1c} and lab HbA_{1c} measurements
- studies that measured POC HbA_{1c} and lab HbA_{1c} more than 7 days apart
- studies that did not compare POC HbA_{1c} and lab HbA_{1c} (reference standard)

Outcome of Interest

- correlation coefficient between POC HbA_{1c} and lab HbA_{1c} measurements

Statistical Analysis

Fisher transformation was performed on correlation coefficients (r) for a bivariate normal distribution using the formula $z = 0.5 * \ln((1 + r)/(1 – r))$, where z denoted the Fisher-transformed r. Standard error for the r was derived from $1/(\sqrt{n – 3})$, where n denoted the sample size. The z then underwent meta-analysis using Stata 12 (Stata Corporation, College Station, Texas). Finally, the summary estimate of z was back-transformed to normal scale using the formula $r = (\exp(2z) – 1)/(\exp(2z) + 1)$. (17)

Quality of Evidence

The quality of evidence for each study was examined using the revised Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2) tool. (18)

The quality of the body of evidence for each outcome was examined according to the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) Working Group criteria. (19) The overall quality was determined to be high, moderate, low, or very low using a step-wise, structural methodology.

Study design was the first consideration; for diagnostic tests, cross-sectional or cohort studies in patients with diagnostic uncertainty and direct comparison of test results with an appropriate reference standard are considered high quality. (20) Five additional factors—risk of bias, inconsistency, indirectness, imprecision, and publication bias—were then taken into account. Limitations in these areas resulted in downgrading the quality of evidence. Finally, 3 main factors that may raise the quality of evidence were considered: the large magnitude of effect, the dose response gradient, and any residual confounding factors. (19) For more detailed information, please refer to the latest series of GRADE articles. (19)

As stated by the GRADE Working Group, the final quality score can be interpreted using the following definitions:

High	High confidence in the effect estimate—the true effect lies close to the estimate of the effect
Moderate	Moderate confidence in the effect estimate—the true effect is likely to be close to the estimate of the effect, but may be substantially different
Low	Low confidence in the effect estimate—the true effect may be substantially different from the estimate of the effect
Very Low	Very low confidence in the effect estimate—the true effect is likely to be substantially different from the estimate of effect

Results of Evidence-Based Analysis

The database search yielded 330 citations published between January 1, 2003, and June 17, 2013 (with duplicates removed). Articles were excluded based on information in the title and abstract. The full texts of potentially relevant articles were obtained for further assessment. Figure 1 shows the breakdown of when and for what reason citations were excluded from the analysis.

Five observational studies met the inclusion criteria. (21-25) The reference lists of the included studies were hand-searched to identify other relevant studies, but with no additional citations were included.

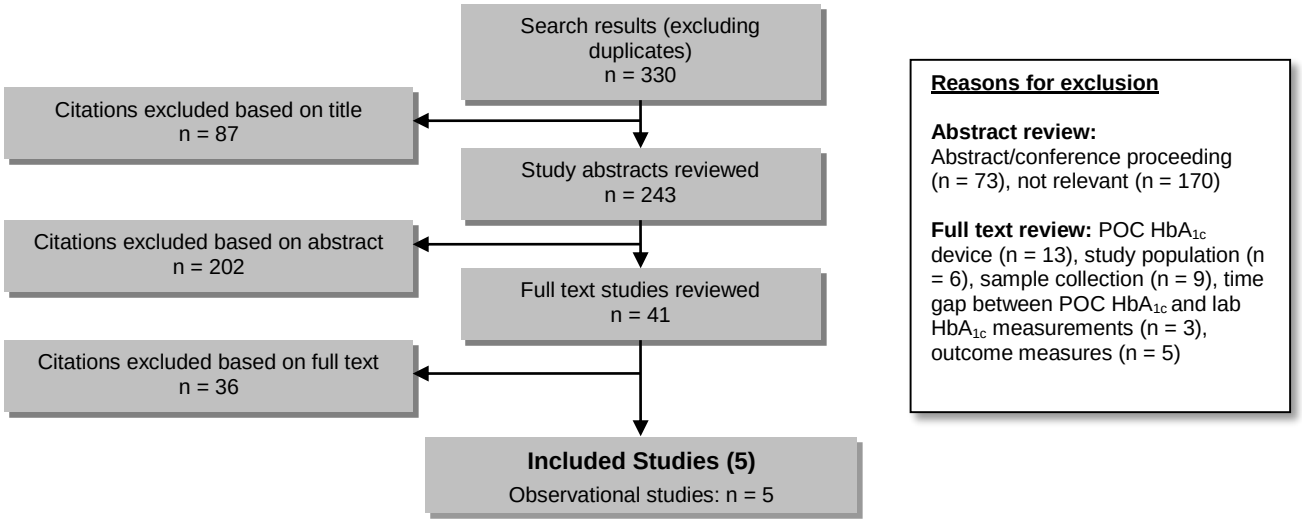

Figure 1: Citation Flow Chart

Abbreviations: lab HbA_{1c}, laboratory hemoglobin A_{1c}; POC HbA_{1c}, point-of-care hemoglobin A_{1c}.

Study authors were contacted for additional information: correlation coefficients, (22;25) time interval between POC HbA_{1c} and lab HbA_{1c} measurements, (25) and whether study participants had diabetes. (24)

For each included study, the study design was identified and is summarized below in Table 3, a modified version of a hierarchy of study design by Goodman. (26)

Table 3: Body of Evidence Examined According to Study Design

Study Design	Number of Eligible Studies
RCTs	
Systematic review of RCTs	
Large RCT	
Small RCT	
Observational Studies	
Systematic review of non-RCTs with contemporaneous controls	
Non-RCT with non-contemporaneous controls	5
Systematic review of non-RCTs with historical controls	
Non-RCT with historical controls	
Database, registry, or cross-sectional study	
Case series	
Retrospective review, modelling	
Studies presented at an international conference	
Expert opinion	
Total	**5**

Abbreviation: RCT; randomized controlled trial.

Correlation Between POC HbA_{1c} and Lab HbA_{1c}

Five cross-sectional studies (21-25) that compared the correlation of POC HbA_{1c} testing with lab HbA_{1c} measurement met the inclusion criteria. All of the included studies measured POC HbA_{1c} using capillary blood samples obtained from a finger prick, and compared this value with the lab HbA_{1c} result measured from venous blood samples. Table 4 summarizes the characteristics of the included studies. The quality of the evidence was moderate (Appendix 2).

Table 4: Characteristics of Included Studies

Author, Year	Study Sample, n	Country	POC HbA_{1c} Device	Reference Test	Time Between POC HbA_{1c} and Lab HbA_{1c} Tests	Industry Sponsorship
Arrendale et al, 2008 (21)	70	USA	A1c Now+	Standard lab HbA_{1c} assays	Within 7 days	—
Leca et al, 2012 (22)	100	France	DCA Vantage	Tosch high-performance liquid chromatography	Within 2 hours	—
Leal et al, 2009 (23)	47	USA	A1c Now+	Standard lab HbA_{1c} assays	Within 4 days	Bayer
Martin et al, 2010 (24)	100	France	In2it	Variant II high-performance liquid chromatography	Within 6 hours	Bio-Rad
Yeo et al, 2009 (25)	80	Singapore	In2it	Cobas c501 latex-enhanced competitive turbidimetric immunoassay	Within 5–15 minutes	—

Abbreviations: HbA_{1c}, hemoglobin A_{1c}; lab HbA_{1c}, laboratory hemoglobin A_{1c}; POC HbA_{1c}, point-of-care hemoglobin A_{1c}.

The correlation coefficients (r) of these 5 studies comparing POC HbA_{1c} testing with lab HbA_{1c} measurement were pooled (Figure 2). Although there was a high correlation between POC HbA_{1c} testing and lab HbA_{1c} measurements among all included studies, there was also a high degree of statistical heterogeneity associated with this analysis. In an attempt to explore the source of the heterogeneity, the meta-analysis was stratified by POC HbA_{1c} device. Between the 2 studies evaluating Bayer's A1cNow+, the pooled correlation coefficient with lab HbA_{1c} was high, and there was no statistical heterogeneity. For the 2 studies on Bio-Rad's In2it, the pooled correlation coefficient was also high, but with significant statistical heterogeneity. One of the potential sources of heterogeneity could be the different lab HbA_{1c} reference standards used in these 2 studies.

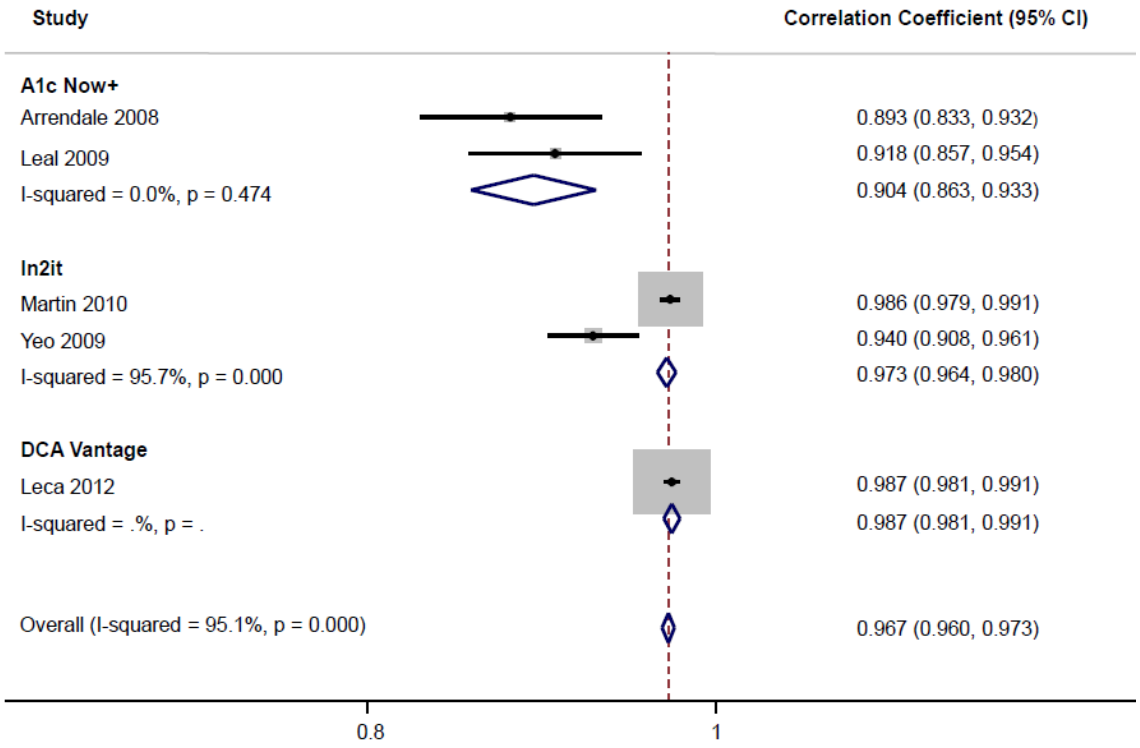

Figure 2: Included Studies Comparing POC HbA_{1c} With Lab HbA_{1c}

Abbreviations: CI, confidence interval; lab HbA_{1c}, laboratory hemoglobin A_{1c}; POC HbA_{1c}, point-of-care hemoglobin A_{1c}.

Limitations

This analysis showed a positive correlation between POC HbA_{1c} testing using capillary blood samples and lab HbA_{1c} measurement using venous blood samples, suggesting a strong agreement between these measurements. However, the results should be interpreted with caution, mainly due to the limitations of the included studies.

It is essential to compare the index test (POC HbA_{1c}) to a standardized and validated reference test (lab HbA_{1c}) to establish the validity of the index test. Laboratory assays employ different biochemical principles to measure HbA_{1c}, including high-performance liquid chromatography based on charge differences of the hemoglobin fractions, and immunoassay based on structural differences. Of the 2 included studies on A1c Now+ (21;23), only "standard central laboratory assays" were reported. The 2 studies on In2it used different reference standards: high-performance liquid chromatography (24) and latex-enhanced competitive turbidimetric immunoassay. (25) Compared to the results from Yeo et al, (25) Martin et al (24) reported a stronger correlation between In2it and the reference standard, both of which were chromatography-based assays.

Correlation coefficient was chosen as the outcome of interest for this review because it was the most commonly reported measure of analytical performance in the literature. Very few studies reported the sensitivity and specificity of POC HbA_{1c} against lab HbA_{1c}. Bland-Altman plot is a preferred method for evaluating agreement between 2 analytical methods. It plots the average (x-axis) against the difference between 2 measurements (y-axis) to show the systematic difference. (27) However, only 2 of the included studies showed a Bland-Altman plot, and both reported a positive bias for POC HbA_{1c} compared to lab HbA_{1c}. (24;25)

A potential bias identified was uncertainty about how participants were selected for the studies, (e.g., randomization, stratification, or consecutive enrolment in a given time period). Another potential source of bias was that POC HbA_{1c} testing involves multiple steps in preparing the blood samples before measurement, and this may increase the risk of measurement errors. The precision of the measurement as measured by coefficient of variation was not consistently reported in the literature.

Although POC HbA_{1c} devices are certified by the NGSP to meet requirements for analytical performance and traceability of results, bias (i.e., difference in the absolute value between POC HbA_{1c} and lab HbA_{1c} measurements) exists. Since the intended use of POC HbA_{1c} for this analysis was for monitoring glycemic control in diabetes (rather than diagnosing diabetes), misclassification was unlikely to be a concern. However, if the POC HbA_{1c} value was close to a threshold at which therapeutic change would be warranted, (e.g., 8.5%), any positive or negative bias may lead to inappropriate treatment decisions. Still, advice on lifestyle modification or dosage change in medications would be unlikely to cause immediate life-threatening harm if patients were monitored closely and had another HbA_{1c} test in 3 months.

Conclusions

Moderate quality evidence showed a positive correlation between POC HbA_{1c} testing and lab HbA_{1c} measurement. Five observational studies compared 3 POC HbA_{1c} devices with lab HbA_{1c} assays, and all reported strong correlation between the 2 tests.

Acknowledgements

Editorial Staff
Jeanne McKane, CPE, ELS(D)

Medical Information Services
Corinne Holubowich, BEd, MLIS
Kellee Kaulback, BA(H), MISt

Expert Advisory Panel on Community-Based Care for Adult Patients With Type 2 Diabetes

Panel Members	Affiliation(s)	Appointment(s)
Co-Chairs		
Dr Baiju Shah	Sunnybrook Health Sciences Centre Institute for Clinical Evaluative Sciences University of Toronto	Staff Physician, Division of Endocrinology Scientist, ICES Associate Professor
Dr David Tannenbaum	Mount Sinai Hospital Ontario College of Family Physicians University of Toronto	Chief of Department of Family & Community Medicine Past-President, OCFP Associate Professor
Endocrinologist		
Dr Harpreet Bajaj	Ontario Medical Association LMC Endocrinology Centre	Tariff Chairman, Section of Endocrinology
Dr Alice Cheng	Trillium Health Partners St. Michael's Hospital	Endocrinologist, Division of Endocrinology and Metabolism
Dr Janine Malcolm	Ottawa Hospital Ottawa Health Research Institute	
Nephrologist		
Dr Sheldon Tobe	Sunnybrook Health Sciences Centre Canadian Cardiovascular Harmonized National Guidelines Endeavor	Associate Scientist Co-Chair, C-CHANGE
Family Physician		
Dr Robert Algie	Fort Frances Family Health Team	Lead Physician
Dr J Robin Conway	Perth and Smiths Falls Community Hospitals Canadian Centre for Research on Diabetes	Family Physician (Diabetes Care)
Dr Lee Donohue	Ontario Medical Association	Health Policy Chair, Section of General and Family Practice
Dr Dan Eickmeier	Huron Community Family Health Team	
Dr Stewart B. Harris	Western University	Professor, Department of Family Medicine

Panel Members	Affiliation(s)	Appointment(s)
Dr Warren McIsaac	Mount Sinai Hospital University of Toronto	
Nurse Practitioner		
Betty Harvey	St. Joseph's Healthcare Hamilton	Clinical Nurse Specialist/Nurse Practitioner, Primary Care Diabetes Support Program
Registered Nurse		
Brenda Dusek	Registered Nurses Association of Ontario	Program Manager, International Affairs & Best Practice Guideline Centre
Registered Nurse/Certified Diabetes Educator		
Bo Fusek	Hamilton Health Sciences Centre	Diabetes Care and Research Program
Melissa Gehring	St. Joseph's Healthcare Hamilton	Diabetes Research Coordinator
Amanda Mikalachki	St. Joseph's Healthcare Hamilton	
Registered Dietitian/Certified Diabetes Educator		
Pamela Colby	St. Joseph's Healthcare Hamilton Brescia University College, Western University	
Stephanie Conrad	Weeneebayko Diabetes Health Program	
Registered Dietitian		
Stacey Horodezny	Trillium Health Partners	Team Leader, Diabetes Management Centre & Centre for Complex Diabetes Care
Lisa Satira	Mount Sinai Hospital	
Pharmacist		
Lori MacCallum, PharmD	Banting and Best Diabetes Centre, University of Toronto	Program Director, Knowledge Translation and Optimizing Care Models Assistant Professor, Leslie Dan Faculty of Pharmacy
Clinical Pharmacist		
Christine Papoushek, PharmD	Toronto Western Hospital University of Toronto	Pharmacotherapy Specialist, Department of Family Medicine
Community Pharmacist		
Mike Cavanagh	Kawartha Lakes Pharmacy Ontario Pharmacists Association	
Economic Modelling Specialist		
Meredith Vanstone, PhD	McMaster University	Post-doctoral Fellow, Centre for Health Economics and Policy Analysis
Epidemiologist/Scientist		
Daria O'Reilly, PhD	McMaster University	Assistant Professor
Knowledge Translation/Delivery of Diabetes Self-Management Education		
Enza Gucciardi, PhD	Ryerson University	Associate Professor, School of Nutrition

Panel Members	Affiliation(s)	Appointment(s)
Bioethicist		
Frank Wagner	Toronto Central CCAC University of Toronto	Assistant Professor, Department of Family and Community Medicine
Ontario Cardiac Care Network Representative		
Kori Kingsbury	Cardiac Care Network	Chief Executive Officer
Heart and Stroke Foundation Representative/Registered Dietitian		
Karen Trainoff	Ontario Heart and Stroke Foundation	Senior Manager, Health Partnerships
Centre for Complex Diabetes Care Representative/Registered Dietitian		
Margaret Cheung	Trillium Health Partners Mississauga Hospital	Clinical Team Leader
Community Care Access Centre Representative		
Dorota Azzopardi	Central West CCAC	Client Services Manager – Quality Improvement, Chronic – Complex and Short Stay
General Internal Medicine/Health Services Research		
Dr Jan Hux	Canadian Diabetes Association	Chief Scientific Officer

Appendices

Appendix 1: Literature Search Strategies

Search date: June 12, 2013
Databases searched: Ovid MEDLINE, MEDLINE In-Process and Other Non-Indexed Citations, EMBASE, All EBM Databases, CINAHL

Q: Point-of-care hemoglobin A1c testing
Limits: 2003–current; English
Filters: none

Database: EBM Reviews - Cochrane Database of Systematic Reviews 2005 to April 2013, EBM Reviews - ACP Journal Club 1991 to May 2013, EBM Reviews - Database of Abstracts of Reviews of Effects 2nd Quarter 2013, EBM Reviews - Cochrane Central Register of Controlled Trials May 2013, EBM Reviews - Cochrane Methodology Register 3rd Quarter 2012, EBM Reviews - Health Technology Assessment 2nd Quarter 2013, EBM Reviews - NHS Economic Evaluation Database 2nd Quarter 2013, Embase 1980 to 2013 Week 23, Ovid MEDLINE(R) 1946 to May Week 5 2013, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations June 11, 2013
Search Strategy:

#	Searches	Results
1	exp Hemoglobin A, Glycosylated/ use mesz,acp,cctr,coch,clcmr,dare,clhta,cleed	24767
2	exp hemoglobin A1c/ use emez	37027
3	(A1c or HbA1c* or h?emoglobin A1c* or glycated h?emoglobin* or glycosylated h?emoglobin* or glycoh?emoglobin*).mp.	91304
4	or/1-3	100156
5	exp Point-of-Care Systems/ use mesz,acp,cctr,coch,clcmr,dare,clhta,cleed	6905
6	exp "point of care testing"/ use emez	3615
7	(point of care or POC or PoCT or near patient test* or bed?side* or DCA Vantage Analyzer* or Smart Direct HbA1c Analyzer* or A1cNow*).mp.	58425
8	or/5-7	58425
9	4 and 8	490
10	limit 9 to english language [Limit not valid in CDSR,ACP Journal Club,DARE,CCTR,CLCMR; records were retained]	468
11	limit 10 to yr="2003 -Current" [Limit not valid in DARE; records were retained]	438
12	remove duplicates from 11	290

CINAHL

#	Query	Results
S1	(MH "Hemoglobin A, Glycosylated")	8,578
S2	(A1c or HbA1c* or h?emoglobin A1c* or glycated h?emoglobin* or glycosylated h?emoglobin* or glycoh?emoglobin*)	12,219
S3	S1 OR S2	12,219
S4	(MH "Point-of-Care Testing")	2,048
S5	(point of care or POC or PoCT or near patient test* or bed?side* or DCA Vantage Analyzer* or Smart Direct HbA1c Analyzer* or A1cNow*)	5,515
S6	S4 OR S5	5,515
S7	S3 AND S6	103
S8	S3 AND S6 Limiters - Published Date from: 20030101-20131231; English Language	96

Appendix 2: Evidence Quality Assessment

Table A1: GRADE Evidence Profile for Comparison of POC HbA_{1c} and Lab HbA_{1c}

Number of Studies (Design)	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Upgrade Considerations	Quality
Correlation Between POC HbA_{1c} and Lab HbA_{1c}							
5 (observational)	Serious limitations (–1)[a]	No serious limitations	No serious limitations[b]	No serious limitations	Undetected	None	⊕⊕⊕ Moderate

Abbreviations: lab HbA_{1c}, laboratory hemoglobin A_{1c}; POC HbA_{1c}, point-of-care hemoglobin A_{1c}.
[a]There was uncertainty in the process of patient selection in most studies, as well as the use of different laboratories for analyses.
[b]In the meta-analysis stratified by POC HbA_{1c} device, there was significant heterogeneity between the studies on In2it, which may have been related to the different reference standards used in these trials. Martin et al (24) reported a stronger correlation between In2it and the reference standard, both of which were based on chromatography; the reference standard used by Yeo et al (25) was an immunoassay.

Table A2: Risk of Bias Among Observational Trials for the Comparison of POC HbA_{1c} and Lab HbA_{1c} (QUADAS-2)

Author, Year	Selection of Participants	Index Test	Reference Standard	Flow and Timing
Arrendale et al, 2008 (21)	High risk[a]	Low risk	Low risk	Low risk
Leca et al, 2012 (22)	High risk[a]	Low risk	Low risk	Low risk
Leal et al, 2009 (23)	Low risk	Low risk	Low risk	High risk[b]
Martin et al, 2010 (24)	High risk[a]	Low risk	Low risk	Low risk
Yeo et al, 2009 (25)	High risk[a]	Low risk	Low risk	Low risk

Abbreviations: lab HbA_{1c}, laboratory hemoglobin A_{1c}; POC HbA_{1c}, point-of-care hemoglobin A_{1c}; QUADAS-2, revised Quality Assessment of Diagnostic Accuracy Studies.
[a]Unclear if participants were selected randomly or consecutively.
[b]Some blood samples were sent to a different laboratory for analysis.

References

(1) Forbes JM, Cooper ME. Mechanisms of diabetic complications. Physiol Rev. 2013 Jan;93(1):137-88.

(2) White NH, Sun W, Cleary PA, Danis RP, Davis MD, Hainsworth DP, et al. Prolonged effect of intensive therapy on the risk of retinopathy complications in patients with type 1 diabetes mellitus: 10 years after the Diabetes Control and Complications Trial. Arch Ophthalmol. 2008 Dec;126(12):1707-15.

(3) Albers JW, Herman WH, Pop-Busui R, Feldman EL, Martin CL, Cleary PA, et al. Effect of prior intensive insulin treatment during the Diabetes Control and Complications Trial (DCCT) on peripheral neuropathy in type 1 diabetes during the Epidemiology of Diabetes Interventions and Complications (EDIC) Study. Diabetes Care. 2010 May;33(5):1090-6.

(4) Holman RR, Paul SK, Bethel MA, Matthews DR, Neil HA. 10-year follow-up of intensive glucose control in type 2 diabetes. N Engl J Med. 2008 Oct 9;359(15):1577-89.

(5) Gallagher EJ, Le RD, Bloomgarden Z. Review of hemoglobin A(1c) in the management of diabetes. J Diabetes. 2009 Mar;1(1):9-17.

(6) Canadian Diabetes Association Clinical Practice Guidelines Expert Committee. Canadian Diabetes Association 2013 clinical practice guidelines for the prevention and management of diabetes in Canada [Internet]. Ottawa, ON: Canadian Diabetes Association; 2013 [cited 2013 Sep 19]. 212 p. Available from: http://guidelines.diabetes.ca/App_Themes/CDACPG/resources/cpg_2013_full_en.pdf

(7) Statistics Canada. Diabetes by sex, provinces and territories [Internet]. Ottawa (ON): Government of Canada; 2013 [cited 2013 Sep 19]. Available from: http://www.statcan.gc.ca/tables-tableaux/sum-som/l01/cst01/health54a-eng.htm

(8) Kost GJ. Guidelines for point-of-care testing. Improving patient outcomes. Am J Clin Pathol. 1995 Oct;104(4 Suppl 1):S111-S127.

(9) John WG, Mosca A, Weykamp C, Goodall I. HbA1c standardisation: history, science and politics. Clin Biochem Rev. 2007 Nov;28(4):163-8.

(10) Sacks DB, Arnold M, Bakris GL, Bruns DE, Horvath AR, Kirkman MS, et al. Guidelines and recommendations for laboratory analysis in the diagnosis and management of diabetes mellitus. Clin Chem. 2011 Jun;57(6):e1-e47.

(11) National Glycohemoglobin Standardization Program. NGSP News [Internet]. Missouri: National Glycohemoglobin Standardization Program; 2013 [cited 2013 Sep 19]. Available from: http://www.ngsp.org/news.asp

(12) National Glycohemoglobin Standardization Program. Obtaining certification [Internet]. Missouri: National Glycohemoglobin Standardization Program; 2013 [cited 2013 Sep 19]. 7 p. Available from: http://www.ngsp.org/cert/Manufinfo1113.pdf

(13) 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 Jan;56(1):44-52.

(14) National Glycohemoglobin Standardization Program. Meeting of the National Glycohemoglobin Standardization Program Steering Committee minutes [Internet]. Missouri: National Glycohemoglobin Standardization Program; 2011 [cited 2013 Sep 19]. 9 p. Available from: http://www.ngsp.org/docs/SC2011.pdf

(15) National Glycohemoglobin Standardization Program. HbA1c Assay Interferences [Internet]. Missouri: National Glycohemoglobin Standardization Program; 2013 [cited 2013 Sep 19]. Available from: http://www.ngsp.org/interf.asp

(16) National Glycohemoglobin Standardization Program. List of NGSP certified methods [Internet]. Missouri: National Glycohemoglobin Standardization Program; 2013 [cited 2013 Sep 19]. 17 p. Available from: http://www.ngsp.org/docs/methods.pdf

(17) Cox NJ. Speaking Stata: Correlation with confidence, or Fisher's z revisited [Internet]. Texas: StataCorp LP; 2008 [cited 2013 Sep 19]. Available from: http://www.stata-journal.com/sjpdf.html?articlenum=pr0041

(18) Whiting PF, Rutjes AW, Westwood ME, Mallett S, Deeks JJ, Reitsma JB, et al. QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies. Ann Intern Med. 2011 Oct 18;155(8):529-36.

(19) Guyatt GH, Oxman AD, Schunemann HJ, Tugwell P, Knottnerus A. GRADE guidelines: a new series of articles in the Journal of Clinical Epidemiology. J Clin Epidemiol. 2011 Apr;64(4):380-2.

(20) Schunemann HJ, Oxman AD, Brozek J, Glasziou P, Jaeschke R, Vist GE, et al. Grading quality of evidence and strength of recommendations for diagnostic tests and strategies. BMJ. 2008 May 17;336(7653):1106-10.

(21) Arrendale JR, Cherian SE, Zineh I, Chirico MJ, Taylor JR. Assessment of glycated hemoglobin using A1CNow+ point-of-care device as compared to central laboratory testing. J Diabetes Sci Technol. 2008 Sep;2(5):822-7.

(22) Leca V, Ibrahim Z, Lombard-Pontou E, Maraninchi M, Guieu R, Portugal H, et al. Point-of-care measurements of HbA(1c): simplicity does not mean laxity with controls. Diabetes Care. 2012 Dec;35(12):e85.

(23) Leal S, Soto-Rowen M. Usefulness of point-of-care testing in the treatment of diabetes in an underserved population. J Diabetes Sci Technol. 2009 Jul;3(4):672-6.

(24) Martin M, Leroy N, Sulmont V, Gillery P. Evaluation of the In2it analyzer for HbA1c determination. Diabetes Metab. 2010 Apr;36(2):158-64.

(25) Yeo CP, Tan CH, Jacob E. Haemoglobin A1c: evaluation of a new HbA1c point-of-care analyser Bio-Rad in2it in comparison with the DCA 2000 and central laboratory analysers. Ann Clin Biochem. 2009 Sep;46(Pt 5):373-6.

(26) Goodman C. Literature searching and evidence interpretation for assessing health care practices. Stockholm, Sweden: Swedish Council on Technology Assessment in Health Care. 1996. 81 p. SBU Report No. 119E.

(27) Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. Lancet. 1986 Feb 8;1(8476):307-10.

Health Quality Ontario
130 Bloor Street West, 10th Floor
Toronto, Ontario
M5S 1N5
Tel: 416-323-6868
Toll Free: 1-866-623-6868
Fax: 416-323-9261
Email: EvidenceInfo@hqontario.ca
www.hqontario.ca

ISSN 1915-7398 (online)
ISBN 978-1-4606-4424-9 (PDF)