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Hemoglobin A_{1c} Testing in Diabetes: A Rapid Review

Health Quality Ontario

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Evidence Development and Standards Branch at Health Quality Ontario

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Conflict of Interest Statement

All authors in the Evidence Development and Standards branch at Health Quality Ontario are impartial. There are no competing interests or conflicts of interest to declare.

Rapid Review Methodology

Rapid reviews are completed in 2–4-week time frames. Clinical questions are developed by the Evidence Development and Standards branch at Health Quality Ontario, in consultation with experts, end users, and/or applicants in the topic area. A systematic literature search is then conducted to identify relevant systematic reviews, health technology assessments, and meta-analyses. The methods prioritize systematic reviews, which, if found, are rated by AMSTAR to determine the methodological quality of the review. If the systematic review has evaluated the included primary studies using the GRADE Working Group criteria (http://www.gradeworkinggroup.org/index.htm), the results are reported and the rapid review process is complete. If the systematic review has not evaluated the primary studies using GRADE, the primary studies in the systematic review are retrieved and the GRADE criteria are applied to 2 outcomes. If no systematic review is found, then RCTs or observational studies are included, and their risk of bias is assessed. All rapid reviews are developed and finalized in consultation with experts.

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 (OHTAC)—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 policy-makers.

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 Health Quality Ontario Publications

To conduct its rapid reviews, 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. Information concerning the health benefits, economic and human resources, and ethical, regulatory, social, and legal issues relating to the intervention may be included to assist in making timely and relevant decisions to optimize patient outcomes.

Disclaimer

This rapid review is the work of the Evidence Development and Standards branch at Health Quality Ontario, and is developed from analysis, interpretation, and comparison of published scientific research. It also incorporates, when available, Ontario data and information provided by experts. As this is a rapid review, it may not reflect all the available scientific research and is not intended as an exhaustive analysis. Health Quality Ontario assumes no responsibility for omissions or incomplete analysis resulting from its rapid reviews. In addition, it is possible that other relevant scientific findings may have been reported since completion of the review. This report is current as of the date of the literature search specified in the Research Methods section. Health Quality Ontario makes no representation that the literature search captured every publication that was or could be applicable to the subject matter of the report. This rapid review 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.

Table of Contents

List of Abbreviations

AACE	American Association of Clinical Endocrinologists
ADA	American Diabetes Association
CADTH	Canadian Agency for Drugs and Technologies in Health
CDA	Canadian Diabetes Association
GRADE	Grading of Recommendations Assessment, Development and Evaluation
HbA_{1c}	Hemoglobin A_{1c}
IDF	International Diabetes Federation
NICE	National Institute of Clinical Excellence
OHTAC	Ontario Health Technology Advisory Committee
RCT	Randomized controlled trial
SEMDSA	Society of Endocrinology Metabolism and Diabetes of South Africa
UKPDS	United Kingdom Prospective Diabetes Study

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

This rapid review aimed to determine the frequency of hemoglobin A_{1c} (HbA_{1c}) testing to assess glycemic control in patients with type 2 diabetes.

Clinical Need and Target Population

Type 2 diabetes accounts for more than 90% of the diabetic population. Optimal control of blood glucose has been shown to decrease the risk of diabetes-related complications. (1) According to the United Kingdom Prospective Diabetes Study (UKPDS), each 1% reduction in HbA_{1c} reduced the risk of microvascular complications by 25% in patients with type 2 diabetes. (1) Hemoglobin A_{1c} has been widely used as a marker of glycemic control to guide treatment decisions, such as lifestyle modification and pharmacotherapy, in clinical practice. (2)

Technology/Technique

Hemoglobin A_{1c} is a fraction of hemoglobin composed mainly of glycohemoglobin. It measures the percentage of hemoglobin that is glycated, i.e., bound by glucose. The value of HbA_{1c} is highly correlated with the concentration of blood glucose. Erythrocytes have a lifespan of approximately 120 days. Glycation occurs over the entire lifespan of erythrocytes. In general, HbA_{1c} reflects the average concentration of blood glucose over the preceding 3 months. (3) In addition to the concentration of blood glucose, disease states that alter the lifespan of erythrocytes, such as renal failure and anemia, could affect the value of HbA_{1c}, resulting in under- or over-estimation of glycemic control. (4)

Ontario Context

In the 2011-2012 fiscal year, more than 3.4 million HbA_{1c} tests were performed in adults older than 18 years of age in Ontario's community laboratories, accounting for approximately $30 million (Cdn). This volume of testing represents an increase of 55% from 2.2 million tests in the 2007-2008 fiscal year. One contributing factor to this upward trend could be the increase in the prevalence of diabetes. (5) More HbA_{1c} tests were performed in women than in men (Table 1, Figure 1). The Ministry of Health and Long-Term Care imposes no cap on the frequency of HbA_{1c} testing.

Table 1: Number of Hemoglobin A_{1c} Tests Performed in Community Laboratories in Ontario Among Adults Older Than 18 Years of Age From Fiscal Year 2007-2008 to Fiscal Year 2011-2012

Fiscal Year	Men, n	Women, n	Total, n
2007-2008	1,103,774	1,116,083	2,219,857
2008-2009	1,368,884	1,456,598	2,825,482
2009-2010	1,515,264	1,614,674	3,129,938
2010-2011	1,561,775	1,650,256	3,212,031
2011-2012	1,679,195	1,793,541	3,472,736

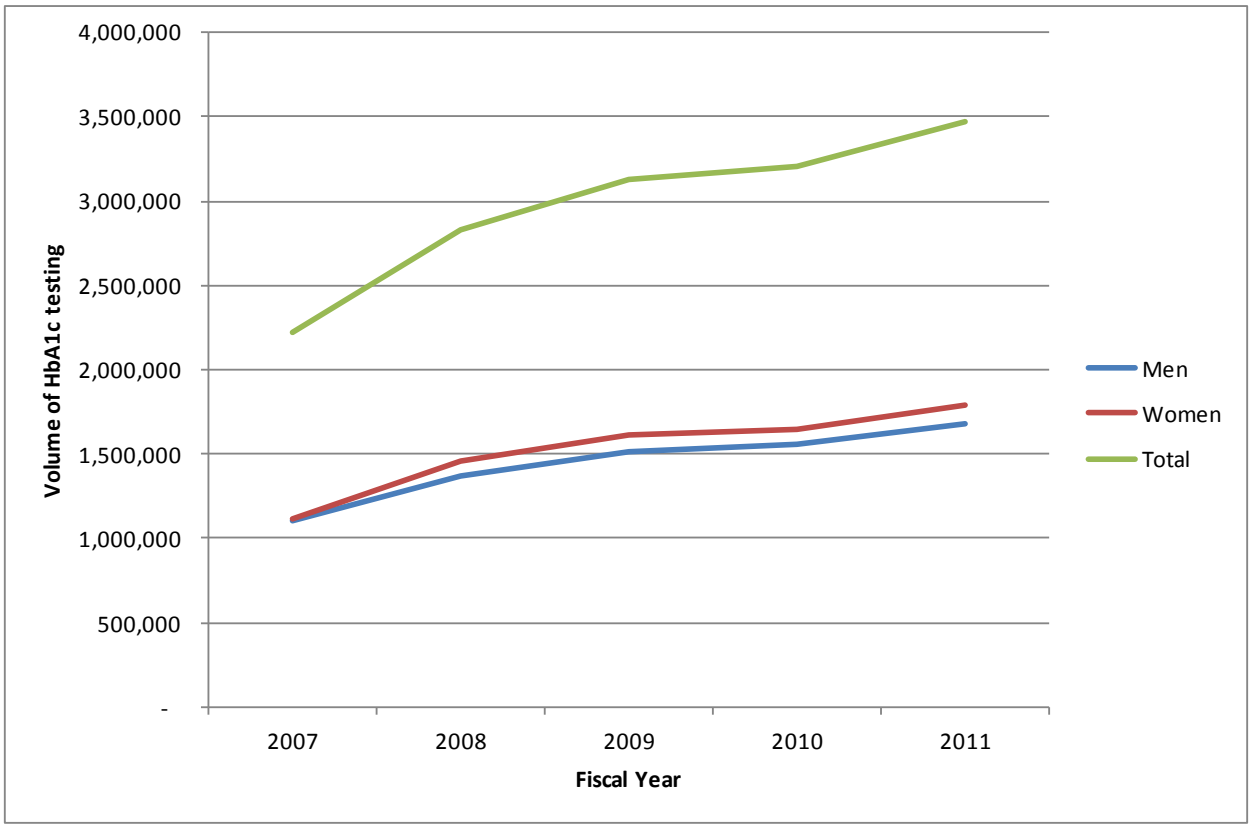

Figure 1: Volume of Hemoglobin A_{1c} Testing in Community Laboratories in Ontario for Adults Older Than 18 Years of Age From Fiscal Year 2007-2008 to Fiscal Year 2011-2012

The number of HbA_{1c} tests per person increased annually from fiscal years 2007-2008 to 2011-2012 (Table 2). Approximately 37,000 persons had HbA_{1c} tested more than 4 times in the 2011-2012 fiscal year (Table 2), and more than 60% of them were aged 65 years or older (Figure 2).

In fiscal year 2011-2012, 783,869 patients had HbA_{1c} tested 2 or more times (Table 2). Assuming a prevalence of type 2 diabetes of 800,000 in Ontario and that every patient has HbA_{1c} tested, then 60,131 (800,000−783,869) patients would have HbA_{1c} tested once yearly. This figure reflects potential underuse of HbA_{1c} testing among this subgroup of patients.

In contrast, on the basis of the same assumptions, approximately 1.4 million (1,463,901−60,131) HbA_{1c} tests were performed on people without diabetes. The World Health Organization recommended using HbA_{1c} to diagnose diabetes in 2011. (6) In the same year, the Canadian Diabetes Association issued a position statement to recommend using HbA_{1c} as a diagnostic test for type 2 diabetes. (7) These recommendations could, in part, account for the increase in use.

Table 2: Number of Hemoglobin A_{1c} Tests per Person Performed in Community Laboratories in Ontario From Fiscal Year 2007-2008 to 2011-2012

	Number of Hemoglobin A_{1c} Tests Per Person					
Fiscal Year	0	1	2	3	4	5+
2007-2008	8,656,842	833,811	260,087	136,372	66,022	32,099
2008-2009	8,398,552	1,170,192	328,448	159,075	76,710	35,938
2009-2010	8,396,075	1,286,742	367,902	178,457	86,782	38,148
2010-2011	8,541,228	1,325,794	380,815	185,589	90,375	35,479
2011-2012	8,560,807	1,463,901	409,153	197,547	96,153	37,016

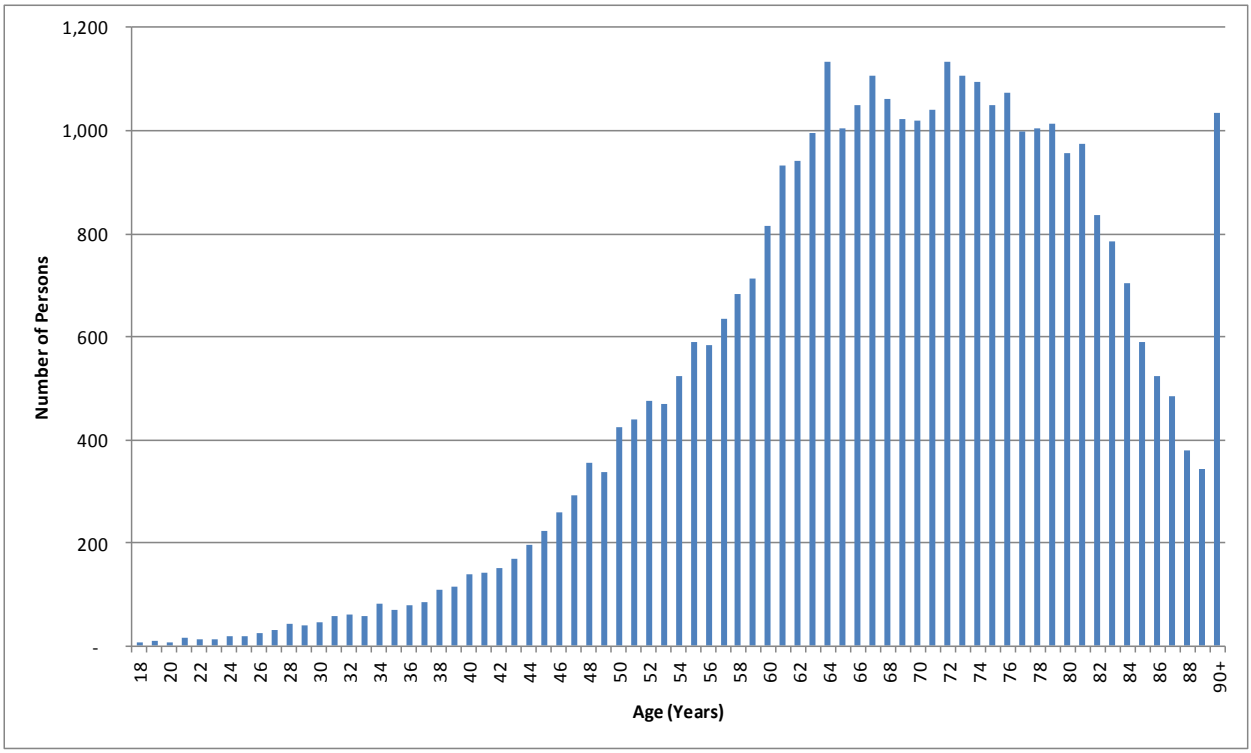

Figure 2: Population by Age With More Than 4 Hemoglobin A_{1c} Tests in Fiscal Year 2011-2012

Rapid Review

Research Question

How often should HbA_{1c} be tested to assess glycemic control in patients with type 2 diabetes?

Research Methods

Literature Search

A literature search for this rapid review was performed on May 2, 2013, using Ovid MEDLINE, Ovid MEDLINE In-Process and Other Non-Indexed Citations, Ovid Embase, EBSCO Cumulative Index to Nursing and Allied Health Literature (CINAHL), the Wiley Cochrane Library, and the Centre for Reviews and Dissemination database, for studies published from January 1, 2008, until May 2, 2013. 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 reports
- published between January 1, 2008, and May 2, 2013
- health technology assessments, systematic reviews, meta-analyses, and clinical practice guidelines
- enrolled patients with type 2 diabetes

Exclusion Criteria

- randomized controlled trials, observational studies, case reports, editorials

Outcomes of Interest

- frequency of HbA_{1c} testing

Expert Panel

In May 2013, an Expert Advisory Panel on Community-Based Care for Adult Patients with Type 2 Diabetes was struck. Members of the panel included physicians, nurses, dietitians, personnel from the Ministry of Health and Long-Term Care, and community representatives.

The role of the Expert Advisory Panel on Community-Based Care for Adult Patients with Type 2 Diabetes was to place into context the evidence produced by Health Quality Ontario and provide advice on community-based care for adult patients in Ontario health care. However, the statements, conclusions, and views expressed in this report do not necessarily represent the views of Expert Advisory Panel members.

Results of Literature Search

The database search yielded 1,654 citations published between January 1, 2008, and May 2, 2013 (with duplicates removed). Articles were excluded on the basis of information in the title and abstract. The full texts of potentially relevant articles were obtained for further assessment.

No systematic reviews or meta-analyses that assessed the frequency of HbA_{1c} testing in patients with type 2 diabetes were identified.

Health Technology Assessments

The Canadian Agency for Drugs and Technologies in Health (CADTH) (8) identified 3 evidence-based guidelines for the frequency of monitoring HbA_{1c} levels in adults with type 2 diabetes, including the National Institute for Health and Clinical Excellence (NICE) in 2009, (9) the Canadian Diabetes Association (CDA) in 2008, (10) and the International Diabetes Federation (IDF) in 2005. (11) The CADTH authors concluded that HbA_{1c} should be measured every 3 months when treatments are being adjusted or glycemic goals are unmet, every 2–6 months until glycemic goals are met, and every 6 months if glycemic control is stable with effective treatment in place.

Clinical Practice Guidelines

Six clinical practice guidelines on the management of diabetes were found. (9;12-16) Table 3 summarizes the guidelines and their recommendations on the frequency of HbA_{1c} testing. These guidelines consistently recommended that HbA_{1c} should be measured every 3 months in diabetic patients not meeting glycemic goals and in those who require treatment changes. For diabetic patients who have stable glycemic control, HbA_{1c} should be measured every 6 months.

Recommendations from the CDA (13), the American Diabetes Association (ADA) (12), the American Association of Clinical Endocrinologists (AACE) (14), and Diabetes Australia (16) were all based on expert consensus. The level of evidence was not listed for the recommendation from NICE. The recommendation from the Society of Endocrinology Metabolism, and Diabetes of South Africa (SEMDSA) (15) were referenced to the ADA guidelines in 2007.

Three (12-14) of the six clinical practice guidelines reviewed were developed for type 1 and type 2 diabetes, while the other 3 (9;15;16) were developed specifically for type 2 diabetes. Therefore, the recommendations on the frequency of HbA_{1c} testing are likely applicable to both types of diabetes.

Table 3: Guidelines for the Assessment of Frequency of Hemoglobin A_{1c} Testing

Guideline, Year	Frequency of Testing	Types of Diabetes	Recommendations	Level of Evidence[a]
CDA, 2013 (13)	Every 3–6 months	All	"For most individuals with diabetes, A_{1c} should be measured every 3 months to ensure that glycemic goals are being met or maintained. Testing at least every 6 months should be performed in adults during periods of treatment and lifestyle stability when glycemic targets have been consistently achieved"	Grade D, Consensus
ADA, 2013 (12)	Every 3–6 months	All	"Perform A_{1c} test at least two times a year in patients who are meeting treatment goals (and who have stable glycemic control). Perform A_{1c} tests quarterly in patients whose therapy has changed or who are not meeting glycemic goals"	Grade E Expert opinion
AACE, 2011 (14)	Every 3–6 months	All	"[Hemoglobin] A_{1c} should be measured at least twice yearly in all patients with diabetes and at least 4 times yearly in patients not at target"	Grade D, No evidence
SEMDSA, 2012 (15)	Every 3–6 months	Type 2	"If the patient's HbA_{1c} is at target and the treatment has not been altered, the HbA_{1c} can be checked every six months. If HbA_{1c} is above the target or the treatment has been altered or intensified, the HbA_{1c} after three months"	Referred to ADA guidelines 2007
Diabetes Australia, 2009 (16)	At least twice a year	Type 2	"Glycated hemoglobin should be measured at least twice a year in people with type 2 diabetes and stable blood glucose control. More frequent testing is required in people with sub-optimal control and following changes to therapy"	Expert consensus
NICE, 2009 (9)	Every 2–6 months	Type 2	"Measure the individual's HbA_{1c} at 2–6 monthly intervals (tailored to individual needs) until the blood glucose level is stable on unchanging therapy; use a measurement made at an interval of less than 3 months as an indicator of direction of change rather than as a new steady state. Six-monthly intervals once the blood glucose level and blood lowering therapy are stable"	Not listed

Abbreviations: AACE, American Association of Clinical Endocrinologists; ADA, American Diabetes Association; CDA, Canadian Diabetes Association; HbA_{1c}, hemoglobin A_{1c}; NICE, National Institute for Health and Clinical Excellence; SEMDSA, Society of Endocrinology Metabolism and Diabetes of South Africa.

[a]Level of evidence according to the specific grading system for each guideline

Conclusions

- The volume of hemoglobin A_{1c} (HbA_{1c}) tests increased annually in Ontario from fiscal years 2007-2008 to 2011-2012.
- Experts conclude that HbA_{1c} should be tested every 3 months when treatments are being adjusted and when glycemic goals are not met in adult patients with diabetes (without hematologic contraindication). Once blood glucose control is stable, HbA_{1c} should be tested every 6 months.
- Hemoglobin A_{1c} should not be measured more than 4 times yearly.
- Recommendations for the frequency of HbA_{1c} testing are applicable to both type 1 and type 2 diabetes.

Acknowledgements

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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 Research Fellow, ICES Assistant 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
Dr William Harper	Hamilton Health Sciences McMaster University	Staff Physician Associate Professor
Dr Janine Malcolm	Ottawa Hospital Ottawa Health Research Institute	Endocrinologist
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	Family Doctor
Dr J Robin Conway	Perth and Smiths Falls Community Hospitals Canadian Centre for Research on Diabetes	Medical Director
Dr Lee Donohue	Ontario Medical Association	Health Policy Chair, Section of General and Family Practice
Dr Dan Eickmeier	Huron Community Family Health Team	Primary Care Physician

Panel Members	Affiliation(s)	Appointment(s)
Dr Stewart B. Harris	Western University	Professor, Department of Family Medicine
Dr Warren McIsaac	Mount Sinai Hospital University of Toronto	Associate Professor and Clinician Scientist
Nurse Practitioner		
Betty Harvey	St. Joseph's Healthcare Hamilton	Clinical Nurse Specialist/Nurse Practitioner
Registered Nurse		
Irmajean Bajnok	Registered Nurses Association of Ontario	Director
Registered Nurse/Certified Diabetes Educator		
Bo Fusek	Hamilton Health Sciences Centre	Clinical Nurse Specialist
Melissa Gehring	St. Joseph's Healthcare Hamilton	Registered Nurse
Amanda Mikalachki	St. Joseph's Healthcare Hamilton	Clinical Diabetes Educator
Registered Dietitian/Certified Diabetes Educator		
Pamela Colby	St. Joseph's Healthcare Hamilton	Registered Dietitian
Stephanie Conrad	Weeneebayko Diabetes Health Program	Registered Dietitian
Registered Dietitian		
Stacey Horodezny	Trillium Health Partners	Team Leader, Diabetes Management Centre & Centre for Complex Diabetes Care
Lisa Satira	Mount Sinai Hospital	Registered Dietitian
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	Clinical Pharmacy Specialist, Ambulatory Care Assistant Professor
Community Pharmacist		
Mike Cavanagh	Kawartha Lakes Pharmacy Ontario Pharmacists Association	Pharmacist/Owner Board of Directors
Economic Modelling Specialist		
Meredith Vanstone, PhD	McMaster University	Post Doctoral Fellow, Centre for Health Economics and Policy Analysis

Panel Members	Affiliation(s)	Appointment(s)
Knowledge Translation/Delivery of Diabetes Education		
Enza Gucciardi, PhD	Ryerson University	Associate Professor
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
Behavioural Scientist/Diabetes Game Changer Initiative Representative		
Dr Michael J Coons	Diabetes Game Changer Initiative York University University of Toronto	Assistant Professor
Ministry of Health and Long-Term Care Representative		
Robert Ock	Health System Accountability and Performance Division	Senior Manager, Implementation

Appendices

Appendix 1: Literature Search Strategies

Search date: May 2, 2013
Databases searched: Ovid MEDLINE, MEDLINE In-Process and Other Non-Indexed Citations, Embase; Cumulative Index to Nursing and Allied Health Literature; Cochrane Library; Centre for Reviews and Dissemination
Limits: 2008-current; English
Filters: Meta-analyses, systematic reviews, health technology assessments, guidelines
Database: Embase 1980 to 2013 Week 17, Ovid MEDLINE(R) 1946 to April Week 4 2013, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations May 1, 2013

Search Strategy:

#	Searches	Results
1	exp Diabetes Mellitus, Type 2/ use mesz	77569
2	exp non insulin dependent diabetes mellitus/ use emez	124647
3	(((ketosis resistant or adult onset or slow onset or maturity onset or non?insulin dependent or type 2 or type II) adj2 (diabet$ or DM)) or (t2dm or NIDDM)).ti.	87919
4	or/1-3	211525
5	exp Hemoglobin A, Glycosylated/ use mesz	20722
6	exp hemoglobin A1c/ use emez	36321
7	(A1c or HbA1c* or h?emoglobin A1c* or glycated h?emoglobin* or glycosylated h?emoglobin* or glycoh?emoglobin*).ti.	9194
8	or/5-7	60153
9	4 and 8	26890
10	Meta Analysis.pt.	39487
11	Meta-Analysis/ use mesz or exp Technology Assessment, Biomedical/ use mesz	48261
12	Meta Analysis/ use emez or Biomedical Technology Assessment/ use emez	81879
13	(meta analy* or metaanaly* or pooled analysis or (systematic* adj2 review*) or published studies or published literature or medline or embase or data synthesis or data extraction or cochrane).ti,ab.	314540
14	((health technolog* or biomedical technolog*) adj2 assess*).ti,ab.	4074
15	exp Standard of Care/ use mesz or exp Guideline/ use mesz or exp Guidelines as Topic/ use mesz	127827
16	exp Practice Guideline/ use emez or exp Professional Standard/ use emez	544004
17	(guideline* or guidance or consensus statement* or standard or standards).ti.	226367
18	or/10-17	1148947
19	9 and 18	2544
20	limit 19 to english language	2362
21	limit 20 to yr="2008 -Current"	1613
22	Case Reports/ or Comment.pt. or Editorial.pt. or Letter.pt.	3925909
23	Case Report/ or Comment/ or Editorial/ or Letter/	5665091
24	or/22-23	5678806
25	21 not 24	1503
26	remove duplicates from 25	1316

Cumulative Index to Nursing and Allied Health Literature

#	Query	Results
S1	(MH "Diabetes Mellitus, Type 2")	29,637
S2	TI (((ketosis resistant or adult onset or slow onset or maturity onset or noninsulin dependent or non-insulin dependent or type 2 or type II) N2 (diabet* or DM)) or (t2dm or NIDDM))	14,522
S3	S1 OR S2	30,731
S4	(MH "Hemoglobin A, Glycosylated")	8,458
S5	TI (A1c or HbA1c* or h?emoglobin A1c* or glycated h?emoglobin* or glycosylated h?emoglobin* or glycoh?emoglobin*)	1,256
S6	S4 OR S5	8,632
S7	S3 AND S6	4,232
S8	(MH "Meta Analysis") or (MH "Systematic Review") or (MH "Practice Guidelines")	68,455
S9	((health technology N2 assess*) or meta analy* or metaanaly* or pooled analysis or (systematic* N2 review*) or published studies or medline or embase or data synthesis or data extraction or cochrane or guideline* or guidance or consensus statement* or standard or standards)	304,508
S10	S8 OR S9	304,508
S11	S7 AND S10	694
S12	S7 AND S11 Limiters - Published Date from: 20080101-20131231; English Language	470

Cochrane

ID	Search	Hits
#1	MeSH descriptor: [Diabetes Mellitus, Type 2] explode all trees	7663
#2	(((ketosis resistant or adult onset or slow onset or maturity onset or non?insulin dependent or type 2 or type II) near/2 (diabet$ or DM)) or (t2dm or NIDDM)):ti (Word variations have been searched)	401
#3	#1 or #2	7792
#4	MeSH descriptor: [Hemoglobin A, Glycosylated] explode all trees	3229
#5	(A1c or HbA1c* or h?emoglobin A1c* or glycated h?emoglobin* or glycosylated h?emoglobin* or glycoh?emoglobin*):ti (Word variations have been searched)	158
#6	#4 or #5	3253
#7	#3 and #6 from 2008 to 2013, in Cochrane Reviews (Reviews and Protocols), Other Reviews, Methods Studies, Technology Assessments and Economic Evaluations	135

Centre for Reviews and Dissemination

Line	Search	Hits
1	MeSH DESCRIPTOR Diabetes Mellitus, Type 2 EXPLODE ALL TREES	676
2	(((ketosis resistant or adult onset or slow onset or maturity onset or non?insulin dependent or type 2 or type II) adj2 (diabet$ or DM)) or (t2dm or NIDDM)):TI	5
3	#1 OR #2	676
4	MeSH DESCRIPTOR Hemoglobin A, Glycosylated EXPLODE ALL TREES	209
5	(A1c or HbA1c* or h?emoglobin A1c* or glycated h?emoglobin* or glycosylated h?emoglobin* or glycoh?emoglobin*):TI	28
6	#4 OR #5	216
7	#3 AND #6	151
8	(#7):TI FROM 2008 TO 2013	101

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