

OPTIMAL THERAPY REPORT

COMPUS
April 2009

Optimal Therapy Recommendations for the
Prescribing and Use of Blood Glucose Test
Strips[DRAFT]

This report is prepared by the Canadian Optimal Medication Prescribing and Utilization Service (COMPUS), a service of the Canadian Agency for Drugs and Technologies in Health (CADTH). This report contains a comprehensive review of existing public literature, studies, materials, and other information and documentation (collectively the “source documentation”) available to CADTH at the time it was prepared, and it was guided by expert input and advice throughout its preparation.

The information in this report is intended to help health care decision-makers, patients, health care professionals, health systems leaders and policymakers make well-informed decisions and thereby improve the quality of health care services. The information in this report should not be used as a substitute for the application of clinical judgment in respect of the care of a particular patient or other professional judgment in any decision making process nor is it intended to replace professional medical advice. While CADTH has taken care in the preparation of the report to ensure that its contents are accurate, complete and up-to-date, CADTH does not make any guarantee to that effect. CADTH is not responsible for any errors or omissions or injury, loss or damage arising from or as a result of the use (or misuse) of any information contained in or implied by the information in this report.

CADTH takes sole responsibility for the final form and content of this report. The statements, conclusions and views expressed herein do not necessarily represent the view of Health Canada or any Provincial or Territorial Government.

Production of this report is made possible through a financial contribution from Health Canada.

Copyright © 2009 CADTH. This Report may be reproduced for non-commercial purposes only and provided appropriate credit is given to CADTH.

Table of Contents

1.0	INTRODUCTION	4
1.1	COMPUS EXPERT REVIEW COMMITTEE	4
2.0	ISSUE	5
2.1	DIABETES MELLITUS	5
2.1.1	<i>Management of blood glucose levels in diabetes mellitus</i>	6
2.1.2	<i>Technology description — self-monitoring of blood glucose</i>	6
3.0	OBJECTIVE	6
4.0	PROJECT OVERVIEW	7
5.0	RESULTS	8
5.1	DRAFT OPTIMAL THERAPY RECOMMENDATIONS	8
5.2	RESEARCH GAPS	10
5.2.1	<i>Populations and comparisons with insufficient evidence</i>	10
5.2.2	<i>Outcomes with limited evidence</i>	10
6.0	THE EVIDENCE	11
7.0	CONSIDERATION OF THE EVIDENCE	11
7.1	CERC PROCESS AND PERSPECTIVE	11
7.2	SPECIFIC CONSIDERATIONS	12
7.2.1	<i>A1C</i>	12
7.2.2	<i>Fasting and post-prandial glycemia</i>	13
7.2.3	<i>Education provided with SMBG</i>	13
7.2.4	<i>SMBG as a component of self-management</i>	13
7.2.5	<i>Consideration of non-randomized studies</i>	14
8.0	NEXT STEPS	14
APPENDIX A: EXPERT COMMITTEE AND CONTRIBUTORS		15
APPENDIX B: DETAILED RECOMMENDATIONS WITH SUPPORTING EVIDENCE		18
BACKGROUND		19
1. ADULTS AND CHILDREN WITH TYPE 1 DIABETES		20
2. ADULTS WITH TYPE 2 DIABETES USING INSULIN		22
3. ADULTS WITH TYPE 2 DIABETES WHO USE ORAL ANTIDIABETES DRUGS		25
4. ADULTS WITH TYPE 2 DIABETES WHO DO NOT USE ANTIDIABETES DRUGS		30
5. WOMEN WITH GESTATIONAL DIABETES		31
CLINICAL FINDINGS OF BLOOD GLUCOSE TEST STRIPS		33
APPENDIX C: DETAILED CERC PROCESS		34
APPENDIX D: ABBREVIATIONS		37
APPENDIX E: GLOSSARY		38

1.0 Introduction

In March 2004, the Canadian Optimal Medication Prescribing and Utilization Service (COMPUS) was launched by the Canadian Coordinating Office for Health Technology Assessment (CCOHTA) — now the Canadian Agency for Drugs and Technologies in Health (CADTH) — as a service to federal, provincial, and territorial jurisdictions and other stakeholders. COMPUS is a nationally coordinated program funded by Health Canada.

The goal of COMPUS is to optimize drug-related health outcomes and cost-effective use of drugs by identifying and promoting optimal drug prescribing and use. Where possible, COMPUS builds on existing applicable Canadian and international initiatives and research. COMPUS goals are achieved through three main approaches:
identifying evidence-based optimal therapy in prescribing and use of specific drugs
identifying gaps in clinical practice, then proposing evidence-based interventions to address these gaps, and
supporting the implementation of these interventions.

Direction and advice are provided to COMPUS through various channels, including the following:

- The COMPUS Advisory Committee (CAC) includes representatives from the federal, provincial, and territorial health ministries and related health organizations.
- The COMPUS Expert Review Committee (CERC) members are listed in Appendix A of this document. The mandate of CERC is advisory in nature and is to provide recommendations and advice to the COMPUS Directorate at CADTH on assigned topics that relate to the identification, evaluation, and promotion of best practices in the prescribing and use of drugs across Canada.
- Stakeholder feedback.

1.1 COMPUS Expert Review Committee

CERC consists of eight Core Members appointed to serve for all topics under consideration during their term of office and three or more Specialist Experts appointed to provide their expertise in recommending optimal therapy for one or more specific topics (Appendix A). For the insulin analogues, and blood glucose test strips, four endocrinologists / diabetes specialists were appointed as Specialist Experts. Two of the Core Members are Public Members who bring a lay perspective to the committee. The remaining six Core Members hold qualifications as physicians, pharmacists, or health economists or have other relevant qualifications, with expertise in one or more areas such as, but not limited to: family practice, internal medicine, institutional or community clinical pharmacy, pharmacoeconomics, clinical epidemiology, drug utilization expertise, methodology, affecting behaviour change (through health professional and/or patient and/or policy interventions), and critical appraisal. The Core Members including Public Members are appointed by the CADTH Board of Directors.

The mandate of CERC is advisory in nature and consists of providing recommendations and advice to CADTH's COMPUS Directorate on assigned topics that relate to the identification, evaluation, and promotion of optimal practices in the prescribing and use of drugs across Canada. CERC develops recommendations and advice with the aim of contributing to optimal health outcomes and fostering a sustainable health care system for Canadians. CERC considers the practical needs of policy makers, health care providers and consumers in implementing and using the recommendations and advice toward the promotion of optimal practices. The overall perspective used by CERC members in producing recommendations is

that of public health care policy makers in pursuit of optimizing the health of Canadians within available health care system resources.

2.0 Issue

CAC has identified management of diabetes mellitus as being a priority area for optimal practice initiatives based on the following criteria:

- large deviations from optimal utilization (overuse or underuse)
- size of patient populations
- impact on health outcomes and cost-effectiveness
- potential to effect change
- benefit to multiple jurisdictions
- measurable outcomes

Within diabetes mellitus management, optimal use of blood glucose test strips in patients with type 1, type 2, and gestational diabetes mellitus was identified by CAC as a priority topic.

Despite widespread use, there is uncertainty regarding the benefits of self-monitoring of blood glucose (SMBG), especially in patients with type 2 diabetes mellitus not using insulin.¹⁻⁴ Moreover, costs associated with self-monitoring of blood glucose are high⁵ and rising steadily⁵⁻⁷ due to the increasing prevalence of type 2 diabetes.⁸ In some publicly-funded drug plans in Canada, blood glucose test strips are among the top five classes in terms of total expenditure,⁵ and more money is often spent on blood glucose test strips than for all oral antidiabetes drugs.^{9,10} In 2006, \$250 million was spent on blood glucose test strips in eight (Newfoundland, Nova Scotia, Quebec, Ontario, Manitoba, Saskatchewan, British Columbia, Non-Insured health benefits Program) publicly-funded drug plans in Canada, while over \$120 million was spent in privately-funded drug plans.^{10*} It is estimated that greater than 50% of the total cost of blood glucose test strips is expended on patients with type 2 diabetes who are not using insulin.¹⁰

2.1 Diabetes Mellitus

Diabetes mellitus is a chronic disease characterized by the body's inability to produce sufficient insulin and/or properly use insulin.¹¹ Type 1 diabetes mellitus occurs in approximately 10% of patients with diabetes, and it results when little or no insulin is produced by the body.¹² Type 2 diabetes mellitus is a metabolic disorder caused by varying degrees of insulin resistance; the body usually produces insulin but is unable to use it properly.¹² When inadequately managed, diabetes is likely to result in poor glycemic control.¹¹ Impaired glycemic control, if prolonged, may result in diabetes-related complications (e.g., ischemic heart disease, stroke, blindness, end-stage renal disease, lower limb amputation).^{13,14}

The global prevalence of diabetes is estimated to be 246 million and is projected to increase to 380 million by 2025.¹⁵ In 2005/2006 approximately 1.9 million (5.9%) Canadians aged 20 years and older had diagnosed diabetes.¹⁶ However, it is estimated that 2.8% of the general adult population has undiagnosed type 2 diabetes mellitus,¹⁷ and the true prevalence of diabetes may approach 2.0 million.¹⁸

*

* Extrapolated from data reported for 67% of privately funded drug plans in Canada.¹⁰

2.1.1 Management of blood glucose levels in diabetes mellitus

One goal of diabetes mellitus management is to maintain control of blood glucose levels in order to reduce the patient's risk of developing long-term diabetes-related complications. Lifestyle modifications (i.e., weight control, proper nutrition, and adequate exercise), the use of medications (e.g., insulin and oral antidiabetic drugs), and SMBG are recommended approaches in improving glycemic control.¹⁷ This project focuses on the use and frequency of blood glucose testing by patients with diabetes.

2.1.2 Technology description — self-monitoring of blood glucose

The purpose of SMBG is to collect detailed information about glucose levels across various time points each day and take appropriate action should those levels be outside the desired range.^{19,20} SMBG requires that patients prick their finger with a lancet device to obtain a small blood sample (0.3 µL to 5 µL).^{19,20} The blood is applied to a reagent strip or blood glucose test strip, and glucose concentration is determined by inserting the blood-laden strip into a reflectance photometer, or an electrochemical sensor.¹⁹ Results, based on an automated reading, are available from the photometer within 5 to 30 seconds.¹⁹ The results can be stored in the glucose meter's electronic memory or recorded in the patient's logbook. It has been suggested that patients can adjust food intake, physical activity, and pharmacotherapy in response to their blood glucose readings and thus are better able to maintain optimal glycemic control on a day-to-day basis.^{19,20}

* Extrapolated from data reported for 67% of privately funded drug plans in Canada.¹⁰

3.0 Objective

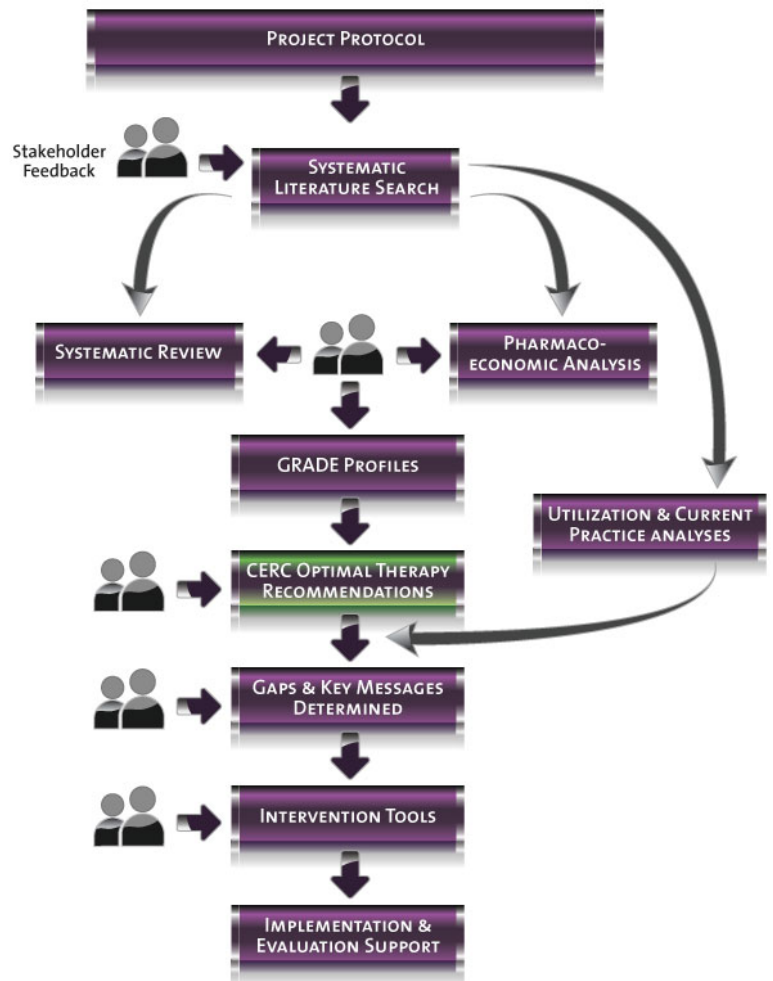
This report provides draft recommendations for the optimal prescribing and use of blood glucose test strips for policy decision makers, health care professionals, and patients.

4.0 Project Overview

Once a topic is selected, COMPUS undertakes activities related to key areas in the COMPUS procedure. The CAC provides advice and guidance throughout the process, from topic identification, through to feedback on recommendations and supporting interventions. CERC, as described in Section 1.1, provides expert advice and recommendations on the topic area relating to the identification, evaluation, and promotion of optimal prescribing and use of medications. A broad range of stakeholders are invited to provide feedback at key stages in the COMPUS process.

To identify and promote the implementation of evidence-based and cost-effective therapy in the prescribing and use of blood glucose test strips for SMBG, COMPUS follows the process outlined in the flow chart to the right.

This report represents the draft optimal therapy recommendations for stakeholder feedback (green box).



5.0 Results

5.1 Draft Optimal Therapy Recommendations

Through careful evaluation of the evidence ([Section 6](#)) and significant deliberation of the issues ([Section 7](#)), CERC produced eight recommendations and suggestions on the use of blood glucose test strips for SMBG in adults with type 1, type 2, and gestational diabetes. CERC applied the Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodology (for developing recommendations ([Section 7](#))). As stipulated by the GRADE method, the strength of a recommendation is reflected by the use of the words “suggests” or “recommends”, (i.e., for a weak recommendation, “CERC **suggests** that...”, and for a strong recommendation, “CERC **recommends** that...”).

A summary of CERC’s draft recommendations/suggestions is presented in Table 1; individual recommendations/suggestions are presented in Table 2. In addition to the recommendations, CERC specified that SMBG should not be applied in isolation; rather, it should be a component of a broader diabetes self-management strategy. Patients for whom SMBG is recommended require education and regular feedback so that blood glucose results are interpreted and applied appropriately.

Table 1: Summary of draft CERC recommendations and suggestions

- For adults and children with diabetes who use insulin, CERC **recommends** that the optimal daily frequency of SMBG be **individualized**.
- For most adults with type 2 diabetes using insulin, CERC **suggests** that the maximum weekly frequency of SMBG is **14 blood glucose test strips per week**.
- For most adults with type 2 diabetes using oral antidiabetes drugs (without insulin) or no antidiabetes drugs, the routine use of blood glucose test strips for SMBG is **not recommended** by CERC.
- For women with gestational diabetes not using antidiabetes drugs, CERC **recommends** that the optimal daily frequency of SMBG be **individualized**.

Detailed information around individual draft CERC recommendations/suggestions (i.e., vote results, the rating of overall quality of clinical evidence, underlying values and preferences related to the recommendations/suggestions, clinical notes, and context) are provided in [Appendix B](#).

Table 2: Individual draft CERC recommendations/suggestions

Population		Recommendation/Suggestion
Type 1 diabetes	Children	<ul style="list-style-type: none"> CERC recommends that the optimal daily frequency of SMBG be individualized for children with type 1 diabetes.
	Adults	<ul style="list-style-type: none"> CERC recommends that the optimal daily frequency of SMBG be individualized for adults with type 1 diabetes.
Type 2 diabetes	Adults using insulin	<ul style="list-style-type: none"> CERC recommends that blood glucose test strips for SMBG be used by most adults with type 2 diabetes using insulin. CERC recommends that the optimal daily frequency of SMBG be individualized for most adults with type 2 diabetes using insulin. CERC suggests that the maximum average weekly frequency of SMBG for most adults with type 2 diabetes using insulin is 14 blood glucose test strips per week.
	Adults using oral antidiabetes drugs (without insulin)	<ul style="list-style-type: none"> Routine use of blood glucose test strips for SMBG is not recommended by CERC for most adults with type 2 diabetes using oral antidiabetes drugs.
	Adults using no antidiabetes drugs	<ul style="list-style-type: none"> Routine use of blood glucose test strips for SMBG is not recommended by CERC for most adults with type 2 diabetes who do not use diabetes pharmacotherapy
Gestational diabetes	Adult women	<ul style="list-style-type: none"> CERC recommends that the optimal daily frequency of SMBG be individualized for most women with gestational diabetes not using antidiabetes drugs.

CERC - COMPUS Expert Review Committee, SMBG – self-monitoring of blood glucose

5.2 Research Gaps

An important aspect of COMPUS' mandate includes the identification and dissemination of research gaps; that is, areas in which there is insufficient evidence to guide optimal prescribing and use. The following sections outline gaps in research related to blood glucose test strips for SMBG. Identification of these gaps will assist researchers and research funding organizations in planning future clinical research. The knowledge that results from such research will lead to improved clinical practice and better outcomes for patients with diabetes.

5.2.1 Populations and comparisons with insufficient evidence

Populations and comparisons for which evidence from randomized controlled trials and/or observational studies was absent are shown in Table 3. First Nations populations were of special interest given the high prevalence of diabetes.⁸ Additional special populations identified by CERC included those for whom hypoglycemia may pose occupational risks (e.g., professional drivers, airline pilots, and construction workers). There were no studies identified comparing the use of SMBG versus no SMBG, or different frequencies of SMBG, in these populations.

Additional populations of interest for which there was no evidence include patients with any of the following characteristics: newly initiated on insulin; with a history of hypoglycemia; experiencing acute illness; undergoing changes in insulin dose/regimen or significant changes in routine; poorly controlled or unstable blood glucose levels; and pregnant or planning a pregnancy.

Table 3: Populations and comparisons for which no evidence was found in the systematic review of blood glucose test strips

Population	SMBG versus no SMBG	SMBG frequency comparisons
Pediatric		
Children with type 1 diabetes	Research question not addressed [†]	No RCTs
Children with type 2 diabetes	No RCTs, No OBS	No RCTs, No OBS
Children with monogenic diabetes	No RCTs, No OBS	No RCTs, No OBS
Adult		
Type 1 diabetes	Research question not addressed [†]	No RCTs
Patients treated with insulin secretagogues	RCT evidence available	No RCTs
Pregnant women type 1 diabetes	Research question not addressed [†]	No RCTs, No OBS
Pregnant women type 2 diabetes	No RCTs, No OBS	No RCTs, No OBS
Patients with gestational diabetes not using diabetes pharmacotherapy	RCT evidence available	No RCTs, No OBS
Patients with gestational diabetes using diabetes pharmacotherapy	No RCTs, No OBS	No RCTs, No OBS
Patients with monogenic diabetes	No RCTs, No OBS	No RCTs, No OBS

[†]SMBG is a standard of care in these populations

RCTs – randomized controlled trials, OBS – observational studies, SMBG – self-monitoring of blood glucose

5.2.2 Outcomes with limited evidence

There was insufficient evidence for a number of outcomes considered important for making recommendations on the use of blood glucose test strips for SMBG. Specifically, there were no studies reporting evidence for the following outcomes: hyperglycemic diabetic ketoacidosis,

patient self-management, macrovascular complications, microvascular complications, and mortality. In addition, A1C was the only outcome available for adults and children with type 1 diabetes, and adults with type 2 diabetes who do not use antidiabetes drugs.

6.0 The Evidence

The clinical evidence for the use of blood glucose test strips for SMBG was derived from the COMPUS Optimal Therapy Report: *Systematic review of use of blood glucose test strips for the management of diabetes mellitus*. Cost-effectiveness data for the use of blood glucose test strips for SMBG were derived from a pharmacoeconomic analysis conducted by COMPUS using the United Kingdom Prospective Diabetes Study (UKPDS) model. The results of those analyses are presented in the Optimal Therapy Report: *Cost-effectiveness of blood glucose test strips in the management of adult patients with diabetes*. Stakeholder feedback was requested and incorporated into both the systematic review and the cost-effectiveness analyses, as directed by CERC.

7.0 Consideration of the evidence

7.1 CERC process and perspective

CERC members consider both clinical effectiveness (i.e., benefits, harms, and burdens) and cost and cost-effectiveness data when formulating recommendations. Committee members bring their individual expertise and experience to bear (as experts, general practitioners, interventionists, consumers, members of the public), and draw upon their own values and preferences to discuss the evidence and reach conclusions.

The process by which draft recommendations are formulated by CERC consists of two main stages. First, the committee considers the clinical evidence regarding safety and effectiveness and draws clinical findings regarding clinically important differences (if any) among the therapies in question. Second, the committee reviews and considers the cost and cost-effectiveness evidence. The sequential consideration of the clinical evidence, followed by the economic evidence, allows for clear delineation of the impact of cost-effectiveness on recommendations, thus increasing transparency of the deliberative process. Optimal therapy recommendations are then formulated based on the efficacy, safety, and pharmacoeconomic data.

CERC develops recommendations and advice with the aim of contributing to optimal health outcomes and fostering a sustainable health care system for Canadians. CERC considers the practical needs of policy makers, health care providers and consumers in implementing and using the recommendations and advice toward the promotion of optimal practices. When possible, guidance is provided for management of specific subgroups of the identified population that may benefit from an alternate approach. To assist in knowledge transfer to intended audiences, the Committee also develops “Clinical notes” to provide guidance based on clinical judgment where there is insufficient evidence. “Context” statements also accompany the recommendations to provide commentary regarding to the evidence.

COMPUS applied the [Grading of Recommendations Assessment, Development and Evaluation \(GRADE\)](#) approach to summarize the available evidence and facilitate the generation of optimal therapy recommendations by CERC.²¹ The GRADE methodology was developed by the GRADE Working Group, an international collaboration of methodologists, to provide committees

charged with formulating recommendations with a framework for evaluating evidence. GRADE provides a systematic and transparent approach to appraise quality of evidence, weigh the balance of benefits versus harms, identify underlying values and preferences, and rate the overall strength of recommendations.²² The GRADE methodology is used by a number of organizations world-wide, including the World Health Organization²³ and the American Thoracic Society.²⁴

The process by which CERC used the GRADE evidence profiles and economic data to generate optimal therapy recommendations for blood glucose test strips consisted of eight steps. Each of these steps is described in further detail in Appendix C.

1. Individual review of GRADE evidence profiles and provision of feedback.
2. Discussion of clinical effectiveness evidence and collated feedback from members.
3. Identification of clinical findings based on clinical evidence of effectiveness and safety.
4. Identification of draft optimal therapy recommendations based on clinical conclusions and cost and cost-effectiveness information.
5. Identification of underlying values and preferences for each recommendation.
6. Appraisal of overall quality of evidence.
7. Grading strength of recommendations.
8. Identification of research gaps.

7.2 Specific Considerations

Prior to initiation of the systematic review by COMPUS, members of CERC identified the outcomes for which evidence was required to make recommendations for the use of blood glucose test strips for SMBG. These included:

- long-term complications of diabetes (e.g., mortality, cardiovascular disease, nephropathy, retinopathy)
- surrogate outcomes related to glycemic control (i.e., A1C, fasting plasma glucose, two-hour post-prandial plasma glucose)
- hypoglycemia
- body weight and body mass index
- quality of life and patient satisfaction
- resource use and costs.

For surrogate outcomes related to glycemic control, a published schema designed by Lassere *et al.* that assessed the validity of surrogate outcomes²⁵ was employed to guide CERC's deliberations.

7.2.1 A1C

A1C was the most frequently reported measure of glycemic control in the studies included in the COMPUS systematic review of blood glucose test strips. During the formulation process for the *Optimal Therapy Recommendations for the Prescribing and Use of Insulin Analogues*,²⁶ (the previous COMPUS topic under diabetes management) CERC deliberated extensively on the evidence available to support the validity of A1C as a surrogate outcome for clinically relevant complications of diabetes,^{13,14,25,27-48} and the minimal difference in this outcome that could be considered clinically relevant.⁴⁹⁻⁵¹ All members of the committee believed there were important limitations associated with the use of A1C as a surrogate outcome. Most felt that A1C was a valid surrogate in trials of type 1 diabetes, especially for microvascular complications. There

was less certainty regarding its validity in type 2 diabetes, especially with respect to cardiovascular outcomes due to the importance of numerous other risk factors such as blood pressure and lipid profile. A minority felt that A1C was an invalid surrogate outcome for both type 1 and type 2 diabetes given the low scores achieved for both conditions according to the surrogate validation schema.²⁵

The committee recognized that the widespread implementation in clinical practice of A1C as a parameter to monitor treatment efficacy in patients with either type 1 or type 2 diabetes has revolutionized diabetes care by allowing for the measurement of long-term glycemic control. Furthermore, diabetes treatment guidelines define optimum glycemic control based on A1C targets. CERC agreed to use a minimal clinically important difference in A1C between 0.7% – 1% during the Committee’s deliberations.

7.2.2 Fasting and post-prandial glycemia

Both fasting and post-prandial glucose scored low according to the validation schema for surrogate outcomes by Lassere *et al.*²⁵ However, CERC recognized that post-prandial blood glucose is increasingly seen as an important target in the treatment of type 2 diabetes due to its potential association with cardiovascular outcomes.

7.2.3 Education provided with SMBG

CERC recognizes performing SMBG is more likely to have a positive impact on diabetes-related outcomes if patients and health care providers take appropriate actions based upon blood glucose readings. Patient education regarding self-interpretation and application was seen by CERC as a key component of SMBG as the available evidence was assessed and recommendations were developed. Because studies varied in the degree to which such education was provided, there was concern that any benefits of SMBG prescribed in combination with patient education may be negated by studies providing insufficient education. To avoid this possibility, subgroup analyses were performed in an attempt to isolate the effect of SMBG prescribed with adequate patient education. The results did not provide enough information for CERC to isolate an effect of education on the available outcomes.

7.2.4 SMBG as a component of self-management

The overall contribution of SMBG as a component of broader self-management strategies is difficult to isolate given the complex and varying nature of the different approaches. In the COMPUS systematic review of blood glucose test strips for SMBG, studies where the patient management strategy was substantially different between comparator arms in aspects not related to SMBG were excluded in the selection process in order to isolate the effects of SMBG. At the request of CERC, a literature search was performed to identify reviews investigating the effectiveness of diabetes self-management strategies, and the role of SMBG within such programs.⁵²⁻⁵⁶ Although no specific evidence related to the benefits of SMBG within self-management programs was identified, the results of these studies helped consolidate the Committee’s view that SMBG should be recommended in conjunction with education and other self-management strategies.

7.2.5 Consideration of non-randomized studies

CERC considered the strengths and weaknesses of the various study designs included in the COMPUS systematic review (i.e., randomized controlled trials, non-randomized trials, time series analysis, retrospective cohort studies, and prospective cohort studies). Non-randomized studies can be defined as any quantitative study estimating the effectiveness of an intervention that does not use randomization to allocate participants to comparator groups.⁵⁷ In comparison with randomized controlled trials, the potential for selection bias and confounding (i.e., distortion in the degree of association between performing SMBG and the outcome of interest) is greater in non-randomized studies. When evaluating the available evidence, CERC identified confounding and selection bias as major limitations of evidence obtained from non-randomized studies.

8.0 Next Steps

The draft recommendations for the use of blood glucose test strips for SMBG are posted for stakeholder feedback for a period of 20 days. CERC will take all feedback into consideration when finalizing the optimal therapy recommendations. Upon completion, these recommendations will be widely disseminated to encourage uptake and implementation by decision makers at various levels (e.g., policy decision makers, health care professionals, and patients). Gaps in practice/knowledge related to the use of blood glucose test strips for SMBG will be identified by comparing the final recommendations to information on current practice (*Current practice analysis: A qualitative analysis of the perceptions of physicians, pharmacists, diabetes-educators, and patients on self-monitoring of blood glucose*) and utilization (*Current utilization of blood glucose test strips in Canada*¹⁰) of these products in Canada.

Key messages to promote the optimal prescribing and use of blood glucose test strips for SMBG will be developed to address identified gaps in practice and knowledge. Intervention tools will be populated with the key messages and related evidence for implementation across Canada.

APPENDIX A: Expert Committee and Contributors

COMPUS Expert Review Committee

Dr. Lisa Dolovich, Chair

Research Director and Associate Professor,
Dept. of Family Medicine, McMaster University
Ambulatory Care Pharmacotherapy Specialist,
St. Josephs Healthcare
Associate Director, Centre for Evaluation of
Medicines

Dr. Mike Evans, Vice Chair

Director, Patient Self Management and Knowledge
Support
Centre for Effective Practice, Department of Family
and Community Medicine, University of Toronto
Director, Health Media Lab, Li Ka Shing Knowledge
Institute
Staff Physician, Toronto Western Hospital
Associate Professor, University of Toronto

Members

Dr. Michael Allen

Associate Professor,
Director, Evidence-based Programs,
Dalhousie University Continuing Medical Education

Dr. Marilyn Caughlin

Family Practitioner

Dr. Scott Klarenbach

Assistant Professor, Department of Medicine,
Division of Nephrology,
University of Alberta
Fellow, Institute of Health Economics

Ms. Cathy MacNutt

Public Member

Mr. Panos Petrides

Public Member

Dr. Adil Virani

Director, Pharmacy Services, Fraser Health
Authority
Associate Professor, Faculty of Pharmaceutical
Sciences, University of British Columbia

Specialist Expert Members

Dr. Marshall Dahl

Clinical Associate Professor,
Division of Endocrinology,
University of British Columbia

Dr. Heather Dean

Professor of Pediatrics and Child Health
Associate Dean (academic), Faculty of Medicine,
Department of Pediatrics, Section of Pediatric
Endocrinology and Metabolism,
University of Manitoba

Dr. S. Ann Colbourne

Director, Division of General Internal Medicine
University of Alberta

Dr. Ehud Ur

Professor of Medicine,
University of British Columbia
Head, Division of Endocrinology,
St. Paul's Hospital and Vancouver General Hospital

Conflicts of Interest

Dr. Lisa Dolovich was co-investigator in studies on behaviour change interventions funded by Merck Frosst Canada Ltd., GlaxoSmithKline Inc., Aventis Pharma Ltd., Eli Lilly Canada Inc., and Crystaal Corporation.

Dr. Michael Evans has received grant support from AstraZeneca Canada to offset the cost of Mini-Med School, an educational program for the public.

Dr. Scott Klarenbach is a member of a research group funded by an unrestricted grant from Amgen Canada and Merck Frosst Canada Ltd. to the Alberta Kidney Disease Network.

Dr. Ann Colbourne has received honoraria for educational lectures for Novo Nordisk Canada Inc., LifeScan, Inc., Sanofi-Aventis Canada Inc., AstraZeneca Canada, Pfizer Canada Inc., and Merck Frosst Canada Ltd. of \$5,000 or less. She was involved in a community-based interprofessional collaborative chronic disease management program, funded by AstraZeneca Canada, Pfizer Canada Inc., and Merck Frosst Canada Ltd.

Dr. Marshall Dahl has received an honorarium for less than \$5,000 from Eli Lilly for his work related to workshops. He has also received an arms-length grant for a diabetes study in coronary artery patients from GlaxoSmithKline Inc. In addition, Dr. Dahl has received an honorarium for less than \$5,000 from Sanofi-Aventis for a lecture.

Dr. Heather Dean has received financial support from Eli Lilly to attend an investigators' meeting on growth hormones in 2005.

Dr. Ehud Ur has received honoraria for educational lectures, honoraria for organizing conferences, or other honoraria for \$5,000 or less from GlaxoSmithKline Inc., Novo Nordisk Canada Inc., Sanofi-Aventis Canada Inc., Merck Frosst Canada Ltd., and Novartis Pharmaceuticals Canada Inc. He has received funding for consultant or advisory services from GlaxoSmithKline Inc. and Novo Nordisk Canada Inc. and has received research grants through the Queen Elizabeth II Foundation (Halifax) from GlaxoSmithKline Inc., Novo Nordisk Canada Inc., and LifeScan, Inc.

None of the other CERC members declared any conflicts of interest. [Conflict of interest guidelines](#) are posted on the CADTH website.

Contributors from COMPUS

Annie Bai, MD, MSc

Advisor, COMPUS Project Quality

Denis Bélanger, BScPhm, ACPR

Director, Topics and Research

Chris Cameron, BSc, EngDip, MSc

Health Economist

Kristen Chelak, BScPhm, MSc, RPh

Research Officer

Avtar Lal, MD, M Phil, PhD

Research Officer

Brendan McIntosh, BSc, MSc

Intermediate Research Officer

Wendy Prichett-Pejic, BSc

Research Assistant

Melissa Severn, MIST

Information Specialist

Sumeet R. Singh, BScPhm, MSc, RPh

Officer, Optimal Practices

Barb Shea, BSP

Vice President, COMPUS

Changhua Yu, MD, MSc

Research Officer

APPENDIX B: Detailed Recommendations with Supporting Evidence

BACKGROUND	19
1. ADULTS AND CHILDREN WITH TYPE 1 DIABETES	20
2. ADULTS WITH TYPE 2 DIABETES USING INSULIN.....	22
3. ADULTS WITH TYPE 2 DIABETES WHO USE ORAL ANTIDIABETES DRUGS	25
4. ADULTS WITH TYPE 2 DIABETES WHO DO NOT USE DIABETES PHARMACOTHERAPY	30
5. WOMEN WITH GESTATIONAL DIABETES.....	31
CLINICAL FINDINGS OF BLOOD GLUCOSE TEST STRIPS.....	33

Background

The detailed recommendation tables offer the following information:

- **Vote results** — Indicates the number of CERC members voting in favour of the proposed [draft recommendation statement](#).
- **CERC rating of overall quality of clinical evidence** — Indicates results of the vote by CERC on the [overall quality of the evidence](#) available for a draft recommendation. Possible ratings of quality were “low”, “moderate”, or “high”, and were based on criteria developed by the GRADE working group.
- **Strength of recommendation** — Indicates the results of the vote by CERC on the [strength of the draft recommendation](#), based on criteria developed by the GRADE working group. Possible ratings are “strong” or “weak”.
- **Underlying values and preferences** — Indicates the [values and preferences](#) that CERC members identified as most important in guiding the draft recommendation.
- **Clinical Note** — Provides guidance from CERC regarding specific clinical considerations that may assist policy decision makers, clinicians, and patients in selecting optimal therapy.
- **Context** — Lists key points arising from CERC’s deliberation of the clinical and economic evidence, as well as clinical issues, pertaining to the draft recommendation. This information is provided to assist clinicians, patients, and policy decision makers with the interpretation and application of the recommendation.
- **Evidence** – The most pertinent evidence used in generating the recommendations is presented following each recommendation table. The detailed evidence profiles for each condition and outcome are presented in the COMPUS Optimal Therapy Reports: *Systematic review of use of blood glucose test strips for the management of diabetes mellitus*⁵⁸ and *Cost-effectiveness of blood glucose test strips in the management of adult patients with diabetes*.⁵⁹

1. Adults and children with type 1 diabetes

CERC **recommends** that the optimal daily frequency of SMBG be individualized for adults and children with type 1 diabetes (*low quality evidence*)

Recommendation voting	Agree	Disagree
Optimal daily frequency of SMBG be individualized for adults	12	0
Optimal daily frequency of SMBG be individualized for children	12	0
Underlying values and preferences		
<ul style="list-style-type: none"> • Primary considerations were improved glycemic control; avoidance of clinically important complications of diabetes and improved patient safety. • Other values and preferences: patient empowerment and self-management; individualization of therapy; recognition of standard of care, and improved quality of life. 		
Clinical Note		
Given a lack of evidence, the following reflects CERC clinical opinion and accepted standards of practice: <ul style="list-style-type: none"> • SMBG is an essential component of diabetes management for adults and children with type 1 diabetes. 		
Context		
<u>Adults</u>		
<ul style="list-style-type: none"> • There was insufficient evidence to make a recommendation regarding optimal or maximum SMBG frequency for this population; however, low quality evidence suggested that performing SMBG a minimum of three times daily was associated with better A1C in comparison with less than three times daily.⁶⁰ • The only RCT data identified⁶¹ were of limited relevance because the SMBG frequencies tested would not be considered acceptable in current clinical practice. • Observational studies are more likely to overestimate the effect of SMBG on A1C despite controlling for potential confounding factors, since individuals who test more frequently may also be more likely to engage in behaviours other than SMBG that improve glycemic control. The effect of different SMBG frequencies on glycemic control cannot be accurately determined under such study conditions. • A1C was the only outcome for which evidence was available. • No cost-effectiveness data were available; only cost per blood glucose test strip was provided. 		
<u>Children</u>		
<ul style="list-style-type: none"> • There was insufficient evidence to make a recommendation regarding optimal or maximum SMBG frequency for this population. • A1C was the only outcome for which evidence was available. • No cost-effectiveness data were available; only cost per blood glucose test strip was provided. 		

Summary of findings table for A1c from comparisons of various SMBG frequencies in adults and children with type 1 diabetes mellitus

Outcome	Number of studies (total sample size)	Effect Estimate MD% (95% CI)	Quality of Evidence
Adults			
Two per day on seven days per week versus four per day once per week	1 RCT ⁶¹ (n = 25)	0.10% (-1.04, 1.24)	Low
Two per day for seven days per week versus four per day on two non-consecutive days per week	1 RCT ⁶¹ (n = 25)	0.10% (-1.01, 1.21)	Low
At least three per day versus one per day	1 R. cohort ⁶⁰ (n = 780)	-0.78% (-1.01, -0.55)	Very Low
Regression coefficient for an average of one additional strip per day	1 R. cohort ⁶² (n = 258 ^b)	-0.661% (P<0.001) ^c	Very Low
Children^d			
Three to four per day versus less than three per day (after three months of SMBG)	1 nRT ⁶³ (n = 60)	-0.6% ^e (-1.13, -0.02)	Very Low
Three to four per day versus less than three per day (after six months of SMBG) ^f	1 nRT ⁶³ (n = 40)	-0.5% ^e (-1.35, 0.34)	Very Low
Economic Evidence			
Unit cost: C\$0.73 per test strip ^g			

A1C - hemoglobin A1C; CI - confidence interval; MD - mean difference; nRT - non-randomized trial; RCT - randomized controlled trial; R. cohort - retrospective cohort; SMBG - self-monitoring of blood glucose

^a Adjusted for age, sex, ethnicity, educational attainment, block group annual income and occupation class, years since diabetes diagnosis, diabetes refill adherence, number of daily insulin injections, clinic appointment "no show" rate, annual eye exam attendance, self reported exercise and diet as diabetes therapy, smoking status, alcohol consumption, and hospitalization and emergency room visit during the baseline year.

^b Children may have been included in this study.

^c Adjusted for age, sex, duration of diabetes, and socioeconomic status. P-value is presented because confidence intervals were not provided.

^d Eight of 60 patients were over 18 years old

^e The mean difference in A1C (95%CI) (SMBG three to four times per day versus SMBG less than three times per day), adjusted for baseline A1C.

^f After six months of SMBG; post diabetes self-management education camp, excluding patients who changed SMBG frequency. The number of adult patients was not reported among 40 patients included in the analysis at six months

^g Due to the low quality of the clinical data, economic evaluations were not performed for adults or children with type 1 diabetes

2. Adults with type 2 diabetes using insulin

CERC **recommends** that SMBG be used and that the optimal daily frequency of SMBG be individualized for **most** adults with type 2 diabetes using insulin. When SMBG has been individualized, CERC **suggests** that the maximum average weekly frequency of SMBG for **most** adults with type 2 diabetes using insulin is 14 tests per week (*low quality evidence*)

Recommendation voting	Agree	Disagree
SMBG be used by most adults	12	0
The optimal daily frequency of SMBG be individualized	12	0
The maximum average weekly frequency of SMBG for most adults is 14 per week	8	4
Underlying values and preferences		
<ul style="list-style-type: none"> • When recommending that most patients perform SMBG, the primary consideration was improved glycemic control and avoidance of clinically important complications of diabetes • For assigning an optimal frequency, the primary considerations were patient empowerment and self-management; and individualization of therapy • For assigning a maximal frequency, the primary consideration was cost-effectiveness. • Other values and preferences: patient empowerment and self-management; improved patient safety; patient choice; and recognition of standard of care; patient choice; recognition of standard of care; validity of available evidence; improved quality of life; patient choice; recognition of standard of care; and lack of strong evidence of clinical benefit 		
Clinical Note		
<p>This population is heterogeneous with respect to the dose and frequency of insulin administration. Given a lack of evidence, the following reflects CERC clinical opinion and accepted standards of practice:</p> <ul style="list-style-type: none"> • Patients who are <u>not</u> identified in the populations below may benefit from performing SMBG less than 14 times per week. • Patients at increased risk of hypoglycemia associated with multiple daily insulin injections (i.e., three or more per day) may benefit from performing SMBG more than 14 times per week. • Populations which may benefit from performing SMBG more than 14 times per week include patients newly initiated on insulin, with a history of hypoglycemia, experiencing acute illness, undergoing changes in insulin dose/regimen or significant changes in routine, who have poorly controlled or unstable blood glucose levels, or who are pregnant or planning a pregnancy 		
Context		
<ul style="list-style-type: none"> • Evidence for this population was limited to A1C and hypoglycemia data obtained from one non-randomized trial⁶⁴ and two observational studies.^{60,65} As a result of such limited evidence, CERC concluded that there was insufficient evidence to make a recommendation regarding optimal SMBG frequency for this population; however, the cost-effectiveness evidence was sufficient to make a recommendation regarding maximal SMBG frequency for this population. • In the cost-effectiveness analysis, there is a clear relationship between the number of blood glucose test strips used per week, modelled benefit in A1C, and ICUR. Thus, while inputs (i.e., benefits of SMBG) are uncertain due to the lack of adequate clinical evidence, relative cost-effectiveness can be elucidated over a plausible range of A1C differences. • The results of the non-randomized trial⁶⁴ may not be generalizable to Canada since the study was conducted in Turkey and the authors studied unusual testing frequencies. As well, results may have been biased since the comparator groups differed from one another at baseline. • Observational studies are likely to overestimate the effect of SMBG on A1C despite controlling for potential confounding factors, since individuals who test more frequently may also be more likely to engage in behaviours other than SMBG that improve glycemic control. Such studies cannot therefore establish that more frequent testing is beneficial. • A1C and hypoglycemia were the only outcomes for which evidence was available. 		

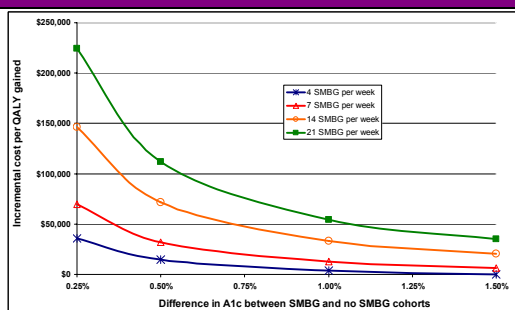
Summary of findings table for adults with type 2 diabetes using insulin

Outcome	Number of studies (sample size)	Effect Estimate (95% CI or P value)	Quality of Evidence
A1C (%)			
Four SMBG per day x one day per week versus no SMBG	1 nRT ⁶⁴ (n = 71)	MD: -1.00% ^a (-1.68, -0.32)	Very Low
Four SMBG per day x once every two weeks versus no SMBG	1 nRT ⁶⁴ (n = 55)	MD: -0.70% ^a (-1.41, 0.01)	Very Low
Four SMBG per day x one day per month versus no SMBG	1 nRT ⁶⁴ (n = 36)	MD: -0.20% ^a (-1.08, 0.68)	Very Low
Four SMBG per day x one day per week versus four SMBG per day x one day every two weeks	1 nRT ⁶⁴ (n = 82)	MD: -0.30% ^a (-0.82, 0.22)	Very Low
SMBG at least once per day versus no SMBG	1 R. cohort ⁶⁰ (n = 4061)	MD: -0.69% ^b (-0.84, -0.54)	Very Low
SMBG less than once per day versus no SMBG	1 R. cohort ⁶⁰ (n = 2541)	MD: -0.13% ^b (-0.30, 0.04)	Very Low
SMBG increased by one strip per day	1 R. cohort ⁶² (n = 290)	-0.108% (p=0.357) ^{c,d}	Very Low
SMBG increased by one strip per day	1 R. cohort ⁶⁶ (n = 245)	-0.65% (p=0.0236) ^{c,e}	Very Low
Overall hypoglycemia			
Four SMBG per day x one day per week versus no SMBG	1 nRT ⁶⁴ (n = 71)	RR: 0.45 ^a (0.03, 6.86)	Very Low
		Rate ratio: 4.04 ^a (0.94, 17.42)	Very Low
Four SMBG per day x once every two weeks versus no SMBG	1 nRT ⁶⁴ (n = 55)	RR: 0.67 ^a (0.04, 10.11)	Very Low
		Rate ratio: 2.67 ^a (0.57, 12.56)	Very Low
Four SMBG per day x one day per month versus no SMBG	1 nRT ⁶⁴ (n = 36)	RR: 0.51 ^a (0.02, 11.74)	Very Low
Four SMBG per day x one day per week versus four SMBG per day x one day every two weeks	1 nRT ⁶⁴ (n = 82)	RR: 0.67 ^a (0.04, 10.39)	Very Low
		Rate ratio: 1.52 ^a (0.66, 3.48)	Very Low
Mortality			
SMBG versus no SMBG	1 P. cohort ⁶⁵ (n = 153)	HR: 0.73 ^f (0.43, 1.26)	Very Low

Economic Evidence

Unit cost: C\$0.73 per blood glucose test strip

Because of the low quality clinical data, cost-effectiveness results were presented for SMBG frequencies of 4, 7, 14, or 21 times weekly, and over a range of plausible A1C effect sizes:



A1C - hemoglobin A1C; CI - confidence interval; HR - hazard ratio; MD - mean difference; nRT - non-randomized trial; OADs – oral antidiabetes drugs; P. cohort - prospective cohort; RR - relative risk; vs. - versus; x - times.

- ^a Baseline patient characteristics including age, sex, disease duration, duration of insulin treatment, hypoglycemia, rate of complications of retinopathy, nephropathy, neuropathy, were significantly different between comparator groups. Unadjusted results were reported
- ^b Adjusted for age, sex, ethnicity, educational attainment, block group annual income, & occupational class, years since diabetes diagnosis, diabetes therapy refill adherence, number of daily insulin injections (insulin users only), clinic appointment 'no show' rate, annual eye exam attendance, self-reported exercise and diet as diabetes treatment, smoking status, alcohol consumption, and hospitalization & emergency room visit during the baseline year
- ^c The decrease in A1C level attributable to one additional SMBG per day
- ^d Unadjusted
- ^e Adjusted for age, sex, region, body mass index, number of months A1C was tested after insulin and number of insulin received
- ^f Adjusted for age, sex, duration of diabetes, prior myocardial infarction, angina, coronary revascularization, diabetes education, A1C, ethnicity (Australian aboriginal)

3. Adults with type 2 diabetes who use oral antidiabetes drugs

Routine use of blood glucose test strips for SMBG is **not recommended** by CERC for **most** adults with type 2 diabetes using oral antidiabetes drugs. (*moderate quality evidence*)

Vote results	Agree	Disagree
	8	4
Underlying values and preferences		
<ul style="list-style-type: none"> • Primary consideration was cost-effectiveness • Other values and preferences: validity of available evidence; improved glycemic control and avoidance of clinically important complications of diabetes; avoidance of potentially detrimental effects of SMBG; improved patient safety; patient choice; patient empowerment and self-management; accessibility of resources to manage diabetes; and lack of strong evidence of clinical benefit 		
Clinical Notes		
<p>Given a lack of evidence, the following reflects CERC clinical opinion and accepted standards of practice:</p> <ul style="list-style-type: none"> • Patients treated with insulin secretagogues may benefit from routine use of SMBG to reduce the risk of hypoglycemia. • Other populations that may benefit from SMBG include those: <ul style="list-style-type: none"> ➢ At increased risk of hypoglycemia (e.g., due to a history of severe hypoglycemia or hypoglycemia unawareness, instances of inadequate caloric intake, unforeseen or unplanned physical activity); ➢ Experiencing acute illness; ➢ Undergoing changes in pharmacotherapy or significant changes in routine; ➢ With poorly controlled or unstable blood glucose levels; ➢ Who are pregnant or planning a pregnancy. 		
Context		
<ul style="list-style-type: none"> • The pooled A1C difference of -0.25% was statistically significant in favour of SMBG in this population, but was not considered clinically significant. The A1C difference between SMBG and no SMBG was similar regardless of whether or not patients were given instructions on the self-interpretation and application of SMBG results. • In the cost effectiveness analysis, based on a pooled A1C difference of -0.25% and the average SMBG frequency used in studies (1.29 tests per day), the ICUR for SMBG versus no SMBG was \$113.6K per QALY gained. CERC members felt that this information supported the clinical finding that SMBG did not provide sufficient benefits to warrant its use by most patients with type 2 diabetes using oral antidiabetes drugs. • For patients who choose to perform SMBG, there is insufficient clinical evidence to recommend an optimal frequency. 		

Summary of findings for A1C from studies comparing SMBG versus no SMBG in adults with type 2 diabetes treated with oral antidiabetes drugs or no antidiabetes drugs

Analysis	Number of studies (sample size)	WMD (95% CI) in A1C (%)	I ² (%)	Quality of Evidence
Evidence from RCTs				
Overall estimate of effect	7 RCTs ^{4,67-72} (n = 2270)	-0.25% (-0.36, -0.15)	0	Moderate
Good quality RCTs only	3 RCTs ^{67,69,71} (n = 1247)	-0.21% (-0.34, -0.08)	0	High
RCTs in which all subjects used OADs	3 RCTs ^{67,68,71} (n = 1628) ^a	-0.24% (-0.36, -0.11)	0	Moderate
RCT in which all patients use sulfonylureas	1 RCT ⁶⁷ (n = 610)	-0.24% (-0.43, -0.05)	N/A	High
More intensive education	3 RCT ⁶⁹⁻⁷¹ (n = 710)	-0.28% (-0.47, -0.08)	17.8	Moderate
Less intensive or unspecified education	5 RCTs ^{4,67,68,71,72} (n = 1712)	-0.22% (-0.34, -0.10)	0	Moderate
Evidence from retrospective cohort studies				
At least one strip per day versus no SMBG	1 R. cohort ⁶⁰ (n = 8735)	-0.68% (-0.77, -0.59) ^b	N/A	Very low
Less than one strip per day versus no SMBG	1 R. cohort ⁶⁰ (n = 10243)	-0.21% (-0.30, -0.12) ^b	N/A	Very low
Prescription of two to four strips per week versus no prescription of strips	1 R. cohort ⁷³ (n = 115)	-0.20% (-0.77, 0.37) ^c	N/A	Very low
Prescription of 0.56 strips per day versus no prescription of strips	1 R. cohort ⁷⁴ (n = 299)	-0.13% (-0.28, 0.02) ^d	N/A	Very low

A1C - hemoglobin A1C; RCT- randomized controlled trial; CI - confidence interval; WMD - weighted mean difference; SMBG - self-monitoring of blood glucose; OADs - oral antidiabetes drugs; N/A - not applicable

^a Farmer *et al* (2007)⁷¹ presented data for a subgroup of patients treated with oral antidiabetes drugs.

^b Data were adjusted for age, sex, ethnicity, educational attainment, annual income & occupational class, years since diabetes diagnosis, diabetes therapy refill adherence, number of daily insulin injections (insulin users only), clinic appointment 'no show' rate, annual eye exam attendance, self-reported exercise and diet as diabetes treatment, smoking status, alcohol consumption, and hospitalization & emergency room visits during the baseline year.

^c Data were not adjusted for any confounder and baseline A1C was not reported; however, age, weight, dose of glyburide, serum creatinine and proteinuria were similar between the two groups.

^d Data were not adjusted for any possible confounders, although baseline A1C, body mass index, chronic illness and disability payment system and ethnicity were similar between the two groups.

Summary of findings for hypoglycemia from RCTs comparing SMBG vs. no SMBG in adults with type 2 diabetes treated with oral antidiabetes drugs or no antidiabetes drugs

Analysis	Number of studies (sample size)	Effect Estimate (95% CI)	I ² (%)	Quality of Evidence
Overall hypoglycemia	3 RCTs ^{67,68,71} (n = 1752)	RR: 1.99 (1.37, 2.89)	33.8	Moderate
	2 RCTs ^{67,69} (n = 794)	Rate ratio: 0.73 (0.55, 0.98)	0	High
Severe hypoglycemia	3 RCTs ^{67,70,71} (n = 1752)	RR: 0.17 ^a (0.01, 4.12)	N/A	Moderate
Nocturnal hypoglycemia	1 RCT ⁶⁷ (n = 610)	RR: 0.41 (0.11, 1.58)	N/A	Moderate

95% CI - 95% confidence intervals; SMBG - self-monitoring of blood glucose; RR - relative risk; RCT - randomized controlled trial; N/A - not applicable

^a Since no events occurred in Guerci *et al* (2003) or Barnett *et al* (2008), only the RR from Farmer *et al* (2007) contributed to the pooled estimate.

Summary of findings for patient reported outcomes from RCTs comparing SMBG versus no SMBG in adults with type 2 diabetes treated with oral antidiabetes drugs or no antidiabetes drugs

Analysis	Number of studies (sample size)	WMD (95% CI)	I ² (%)	Quality of Evidence
DTSQ	2 RCTs ^{68,75} (n = 562)	-0.26 (-1.38, 0.86)	0	Low
WBQ - 12	1 RCT ⁷⁵ (n = 339)	-0.85 (-2.27, 0.56) ^a	N/A	Moderate
WBQ - 22	1 RCT ⁷⁶ (n = 223)	1.83 (-0.05, 3.71) ^a	N/A	Moderate
EuroQol – 5D				
Overall	1 RCT ⁷⁷ (n = 453)	-0.06 (-0.13, 0.02) ^a	N/A	High
Less intensive education	1 RCT ⁷⁷ (n = 302)	-0.029 (-0.084, 0.025) ^a	N/A	High
More intensive education	1 RCT ⁷⁷ (n = 301)	-0.072 (-0.127, -0.017) ^a	N/A	High

DTSQ - Diabetes Treatment Satisfaction Questionnaire; RCT- randomized controlled trial; SMBG - self-monitoring of blood glucose; WBQ - well-being questionnaire; WMD - weighted mean difference

^a mean difference (95% confidence interval)

Summary of findings for long-term complications from studies comparing SMBG versus no SMBG in adults with type 2 diabetes treated with oral antidiabetes drugs or no antidiabetes drugs

Analysis	Number of studies (sample size)	Effect Estimate (95% CI)	I ² (%)	Quality of Evidence
All-cause mortality (newly diagnosed patients)	1 R. cohort ⁷⁸ (n = 2515)	HR: 0.58 ^a (0.35, 0.96)	N/A	Very low
All-cause mortality (previously diagnosed patients)	1 P. cohort ⁶⁵ (n = 1127)	HR: 1.20 ^b (0.94, 1.52)	N/A	Very low
Nonfatal events ^c	1 R. cohort ⁷⁸ (n = 2515)	HR: 0.72 ^a (0.52, 0.999)	N/A	Very low

CI - confidence interval; N/A - not applicable; RCT - randomized controlled trial; WMD - weighted mean difference; HR - hazard ratio; MD - mean difference; P. cohort - prospective cohort; RR - relative risk; R. cohort - retrospective cohort

^a Results adjusted for age, sex, concomitant disease at diabetes diagnosis (hypertension, coronary heart disease, history of stroke), laboratory values (fasting blood glucose, triglycerides), treatment, qualification of the treating physician (general practitioner, internist), centre size (number of newly diagnosed patients with type 2 diabetes during 1995-1999), centre location (small town, city), patient's habitation (small town, city) and patient's health insurance (public, private).

^b Results adjusted for age, sex, duration of diabetes, prior coronary heart disease, cardiovascular disease, peripheral arterial disease, neuropathy, retinopathy, albumin/creatinine ratio, abdominal obesity (negative), use of lipid-lowering medications (negative), Australian Aboriginal, and current smoker status.

^c Myocardial infarction, stroke, foot amputation, blindness in one or both eyes, or end stage renal disease requiring dialysis.

Summary of A1C findings for studies comparing different SMBG frequencies in adults with type 2 diabetes treated with oral antidiabetes drugs or no antidiabetes drugs

SMBG frequency		Number of studies (sample size)	Effect size (95% CI or p value)	Quality of Evidence
Evidence from RCT				
SMBG once per week versus SMBG four times per week		1 RCT ⁷⁹ (n = 178)	MD: -0.08% (-0.41, 0.25)	Moderate
Evidence from retrospective cohort studies				
Average daily SMBG: once per day versus less than once per day		1 R. cohort ⁶⁰ (n = 6594)	MD: -0.47% (-0.57, -0.37) ^a	Very low
SMBG increased by one strip per day	Patients using OADs	1 R. cohort ⁶⁶ (n = 1795)	0.09% (p = 0.5392) ^b	Very low
	Patients using sulfonylureas	1 R. cohort ⁸⁰ (n = 216)	0.02% (p > 0.50) ^c	Very low
	New users of SMBG	1 R. cohort ⁸¹ (n = 5546)	-0.42% (p < 0.0001) ^d	Very low
	Prevalent users of SMBG	1 R. cohort ⁸¹ (n = 7409)	-0.16% (p < 0.0001) ^e	Very low
SMBG increased by 10 test strips per week		1 R. cohort ⁸² (n = 5962)	-0.06 (0.01) ^f (p = 0.38)	Very low

95% CI – 95% confidence interval; MD – mean difference; OADs – oral antidiabetes drugs; RCT – randomized controlled trial; SMBG - self-monitoring of blood glucose

^a Data adjusted for age, sex, ethnicity, educational attainment, block group attainment, block group annual income and occupation class, years since diabetes diagnosis, diabetes therapy refill adherence, clinic appointment “no show” rate, annual eye exam attendance, self-reported exercise and diet as diabetes therapy, smoking status, alcohol consumption, and hospitalization and emergency room visits during the baseline year.

^b Adjusted for age, sex, region, body mass index, months since initiation of oral antidiabetes drugs and A1C test, number of oral medications received in six months prior to A1C test.

^c Adjusted for age, daily glyburide dose, serum creatinine concentration, urine protein content, hospital admissions, number of providers, number of ophthalmology visits, number of diabetes clinic visits.

^d Data adjusted for prebaseline A1C (last A1C prior to baseline), sex, age, inpatient comorbidity score, diabetes refill medication adherence, diabetes therapies, appointment “no show” rate, performance of annual ophthalmology exams, prebaseline rates of hospital, emergency room, primary care and specialty visits, primary care provider type, smoking status, neighbourhood level, median family income, residence in a poorly educated neighbourhood, residence in a predominately working-class neighbourhood, and the length of time between pre and post-A1C tests.

^e Data adjusted as in footnote 'd' but also for: SMBG, daily insulin injection frequency, appointment 'no show' rate, inpatient comorbidity score, and inpatient/outpatient utilization

^f Coefficient (standard error) represents change in A1c for every ten glucose test strips used each week. Coefficients are derived for each outcome stratum using separate multivariate linear regression models adjusting for initial doses of glyburide and metformin and the number of oral antidiabetes drugs

Summary of economic findings for the comparison of SMBG versus no SMBG for adults with type 2 diabetes in adults using oral antidiabetes drugs or no antidiabetes drugs

All patients on OAD(s) or no diabetes pharmacotherapy			
	Δcost (C\$)	ΔQALYs	ICUR (C\$/QALY)
Reference Case			
WMD in A1C of -0.25 (-0.36, -0.15) favouring SMBG. Effect estimate derived using overall estimate of effect from seven RCTs ^{4,67-72}	\$2,711	0.02385	\$113,643/QALY
Probability SMBG is cost-effective at willingness to pay of \$50,000 per QALY = 2% Probability SMBG is cost-effective at willingness to pay of \$100,000 per QALY = 40%			
One-way sensitivity analyses			
WMD in A1C of -0.21 (-0.34, -0.08) favouring SMBG. Effect estimate derived from three good quality RCTs ^{67,69,71}	\$2,735	0.02043	\$133,829/QALY
ΔA1C estimate of -0.68 (-0.77, -0.59) favouring SMBG. Effect estimate derived from a poor-quality observational study ⁶⁰	\$2,523	0.05311	\$47,512/QALY
ΔA1C estimate of -0.28 (-0.47, -0.08) favouring SMBG. Effect estimate derived from two good-quality RCTs ^{69,71} and one poor-quality RCT ⁷⁰ where patients used more intensive education	\$2,694	0.02696	\$99,916/QALY

Δ - change; C\$ - Canadian dollars; ICUR - incremental cost-utility ratio; quality-adjusted life-years; RCT - randomized controlled trial; SMBG - self-monitoring of blood glucose

4. Adults with type 2 diabetes who do not use antidiabetes drugs

Routine use of blood glucose test strips for SMBG is **not recommended** by CERC for most adults with type 2 diabetes who do not use diabetes pharmacotherapy (*low quality evidence*)

Vote results	Agree	Disagree
	9	2
Underlying values and preferences		
<ul style="list-style-type: none"> Primary consideration was cost for payers Other values and preferences: validity of available evidence; patient choice; patient empowerment and self-management; avoidance of potentially detrimental effects of SMBG; improved quality of life; individualization of therapy; accessibility of resources to manage diabetes; lack of strong evidence of clinical benefit and limited RCT evidence supporting the benefits of SMBG in this patient population. 		
Clinical Note		
<p>Given a lack of evidence, the following reflects CERC clinical opinion and accepted standards of practice:</p> <ul style="list-style-type: none"> Women with type 2 diabetes who are not using insulin and are considering a planned pregnancy may benefit from SMBG testing. 		
Context		
<ul style="list-style-type: none"> In the cost effectiveness analysis, based on the statistically non-significant A1C difference of -0.05% in favour of SMBG observed in the RCT⁷¹ and the average SMBG testing frequency of 0.71 per day, the ICUR for SMBG versus no SMBG was \$291.1K per QALY gained. CERC members felt that this information supported the clinical finding that SMBG did not provide sufficient benefits to warrant its use by most patients with type 2 diabetes who do not use antidiabetes drugs. A1C was the only outcome for which evidence was available. 		

Summary of findings for outcomes from studies comparing of SMBG versus no SMBG for adults with type 2 diabetes in adults using no antidiabetes drugs

Outcome	Number of studies (sample size)	Effect Estimate MD (95% CI)	Quality of Evidence
A1C (%) change from baseline	1 RCT ⁷¹ (n = 124)	-0.05 (-0.33, 0.23)	Moderate
A1C (%) at end			
SMBG at least once per day versus no SMBG	1 R. cohort ⁶⁰ (n = 3445)	-0.64 ^a (-0.81, -0.47)	Very Low
SMBG less than once per day versus no SMBG	1 R. cohort ⁶⁰ (n = 4198)	-0.34 ^b (-0.47, -0.21)	Very Low
Economic Information			
Unit cost: C\$0.73 per test strip ICUR - diet only, RCT data ^c : C\$292,144 per QALY gained ($\Delta C = C\$1,372$; $\Delta QALYs = 0.00470$)			

A1C - hemoglobin A1C; RCT- randomized controlled trial; R. cohort - retrospective cohort; CI - confidence interval; MD - mean difference; ΔC - difference in costs between strategies; $\Delta QALY$ - difference in QALYs gained between strategies, QALY - quality adjusted life-year; ICUR - incremental cost-utility ratio

^a Adjusted for age, sex, ethnicity, educational attainment, block group annual income, occupational class, years since diabetes diagnosis, diabetes therapy refill adherence, number of daily insulin injections, (insulin users only), clinic appointment 'no show' rate, annual eye exam attendance, self-reported exercise and diet as diabetes treatment, smoking status, alcohol consumption, and hospitalization & emergency room visit during the baseline year.

^b Initiating once daily monitoring resulted in lowering of A1C concentration by 0.35% ($p < 0.0001$). Models were adjusted for prebaseline A1C, sex, age, inpatient comorbidity score, diabetes refill medication adherence, diabetes therapies (therapeutic class), appointment "no show" rate, performance of annual ophthalmology exams, prebaseline rates of hospital, emergency room, primary care and specialty visits, primary care provider type, smoking status, neighborhood level, median family income, residence in a poorly educated neighborhood, residence in a predominately working-class neighborhood, and the length of time between pre and post-A1C tests.

^c Baseline A1C = 7.48%; mean age = 66 years; duration of diabetes = three years; frequency = 0.71 test strips per day; WMD = -0.05 (-0.33, 0.23); time horizon = 40 years.

5. Women with gestational diabetes

CERC **recommends** that the optimal daily frequency of SMBG be individualized for most women with gestational diabetes not using diabetes pharmacotherapy. (*low quality evidence*)

Vote results	Agree	Disagree
	10	1
Underlying values and preferences		
<ul style="list-style-type: none"> • Primary considerations were reduced fetal/neonatal complications, improved glycemic control, and avoidance of clinically important complications of diabetes • Other values and preferences: patient empowerment and self-management; individualization of therapy; improved patient safety; recognition of standard of care 		
Clinical Note		
<p>Given a lack of evidence, the following reflects CERC clinical opinion and accepted standards of practice:</p> <ul style="list-style-type: none"> • SMBG should be performed by women with gestational diabetes using insulin or oral antidiabetes drugs. 		
Context		
<ul style="list-style-type: none"> • There was insufficient evidence to make a recommendation regarding optimal or maximum SMBG frequency for this population. • The only statistically significant results in favour of SMBG in the RCT⁸³ were reduced risks for birth weight greater than 90th percentile [RR (95% CI) = 0.43 (0.20, 0.92)] and hyperbilirubinemia [RR (95% CI) = 0.51 (0.26, 0.99)] in the subgroup of women who had a one-hour post-breakfast blood glucose of ≥ 7.8 mmol/L. Then, 25% of patients in both arms started using insulin during the trial because their glycemic target was not achieved. • No cost effectiveness data were available; only cost per strip was provided. 		

Summary of findings from RCTs comparing SMBG versus no SMBG in women with gestational diabetes

Outcome	Number of studies (total sample size)	Effect Estimate (95% CI)	Quality of Evidence
Fasting blood glucose (mmol/l)	1 RCT ⁸³ (n = 58)	MD: -0.22 (-0.55, 0.11)	Low
One-hour post-prandial blood glucose (mmol/l)	1 RCT ⁸³ (n = 58)	MD: 0.47 (-0.12, 1.06)	Low
Weight gain (kg)	1 RCT ⁸³ (n = 58)	MD: -2.50 (-6.16, 1.16)	Low
Self-efficacy at 37 weeks (Diabetes Empowerment Scale) ^a	1 RCT ⁸³ (n = 58)	MD: 3.70 (-1.56, 8.96)	Low
Caesarean section	2 RCTs ^{83,84} (n = 400)	RR: 1.18 (0.61, 2.27)	Low
Birth trauma	1 RCT ⁸³ (n = 58)	RR: 0.87 (0.06, 13.27)	Low
All cause fetal mortality	2 RCTs ^{83,84} (n = 400)	RR: 1.46 (0.18, 11.59)	Low
Gestational age at delivery (weeks)	2 RCTs ^{83,84} (n = 400)	WMD: -0.05 (-0.35, 0.25)	Low
Hypoglycemia (not classified)	2 RCTs ^{83,84} (n = 391)	RR: 0.64 (0.39, 1.06)	Low
Macrosomia (birth weight > four kg)	1 RCT ⁸⁴ (n = 342)	RR: 0.94 (0.53, 1.67)	Moderate
Birth weight > 90 th percentile	2 RCTs ^{83,84} (n = 400)	RR: 0.82 (0.50, 1.37)	Low
Birth weight < 10 th percentile	1 ⁸⁴ (n = 342)	RR: 1.19 (0.53, 2.67)	Moderate
Respiratory complications	1 RCT ⁸³ (n = 58)	RR: 0.87 (0.06, 13.27)	Low
Hospitalization (neonatal intensive care)	1 RCT ⁸³ (n = 58)	RR: 0.87 (0.13, 5.77)	Low
Apgar score - one minute	1 RCT ⁸³ (n = 58)	MD: -0.40 (-1.51, 0.71)	Low
Apgar score - five minutes	1 RCT ⁸³ (n = 58)	MD: -0.20 (-1.13, 0.73)	Low
Hyperbilirubinemia	2 RCTs ^{83,84} (n = 369)	RR: 0.64 (0.39, 1.04)	Low
Economic Information			
Unit Cost: C\$0.73 per test strip			

95% CI – 95% confidence interval; MD - mean difference; PBBG - post-breakfast blood glucose; RCT- randomized controlled trial; RR - relative risk; WMD - weighted mean difference

^a Lower scores indicate greater self-efficacy.

^b No fetal death was reported in either arm

^c Author reported p < 0.05

^d 25% of patients in both arms started using insulin during the trial because glycemic target was not achieved

Clinical findings of blood glucose test strips

The following clinical findings, which represent an **intermediate step in the CERC deliberative process**, are derived solely from CERC's considerations of clinical evidence regarding blood glucose test strips. Economic evidence was not considered at this stage. Therefore, they **do not represent CERC's recommendations and suggestions** for the optimal prescribing and use of blood glucose test strips. CERC's optimal therapy recommendations for blood glucose test strips are presented in summary form (Section 5.1) and detailed form (Appendix B).

Patients who use insulin

For adults with type 1 diabetes:

- the optimal daily frequency of SMBG should be individualized for most adults with type 1 diabetes

For children with type 1 diabetes:

- the optimal daily frequency of SMBG should be individualized for most children with type 1 diabetes

For adults with type 2 diabetes:

- blood glucose test strips for SMBG should be used by most adults with type 2 diabetes using insulin
- the optimal daily frequency of SMBG should be individualized with adults with type 2 diabetes using insulin.

Patients who do not use insulin

For adults with type 2 diabetes:

- routine SMBG by most adults with type 2 diabetes using oral anti-diabetes drugs is not recommended/suggested by CERC.
- routine SMBG by most adults with type 2 diabetes not using diabetes pharmacotherapy is not recommended/suggested by CERC.

Gestational diabetes

For women with gestational diabetes who do not use pharmacotherapy:

- most women with gestational diabetes should use blood glucose test strips for SMBG. The Canadian Diabetes Association 2008 guidelines recommend that SMBG should be conducted four or more times daily, both pre- and post-prandially.
- the management of gestational diabetes differs significantly from that of diabetes that exists prior to conception.

APPENDIX C: Detailed CERC Process

The steps that CERC followed for generating draft optimal therapy recommendations are presented here.

1. Individual review of GRADE evidence profiles and provision of feedback

CERC members were provided with the GRADE evidence profiles and a graphical summary of the results presented in the profiles. Committee members completed a feedback form for each GRADE evidence profile. Feedback was collated and provided to CERC members in advance of the Committee meeting.

2. Discussion of clinical-effectiveness evidence and collated feedback from members

CERC members discussed the evidence presented in the GRADE evidence profiles and the associated feedback. Context and clinical issues raised during the discussion were recorded for each evidence profile. GRADE Summary of Findings tables, which were created to reflect the body of generated information, contained:

- results from the GRADE evidence profiles
- draft clinical findings
- summary of values and preferences expressed by CERC members
- summary of feedback on the criteria used to assess strength of recommendations.

3. Identification of clinical findings based on clinical evidence of effectiveness and safety

Each member of CERC participating in the meeting voted for one clinical finding statement, the two most important values or preferences that guided their choice, and the overall quality of the available evidence. Points of discussion relating to the clinical finding statement were documented as context. A summary of the clinical findings is provided in Appendix B.

4. Identification of draft optimal therapy recommendations based on clinical conclusions and cost/cost-effectiveness information

CERC reviewed and discussed the results from the pharmacoeconomic analyses conducted by COMPUS. Where one treatment strategy appeared to be more effective than the alternative, CERC assessed whether the increase in cost associated with the increase in effectiveness represented reasonable “value for money”. There is no empirical basis for assigning a value (or values) to the cut-off between cost-effectiveness and cost ineffectiveness.

Conclusions from the pharmacoeconomic analyses were added to the GRADE Summary of Findings tables. Costing data were supplied where cost-effectiveness results were not available. Draft optimal therapy recommendations, reflecting both clinical and cost/cost-effectiveness results, were prepared as a starting point for CERC’s deliberation and voting. Voting was conducted by secret ballot and web voting. Quorum consisted of a minimum of five core CERC members, and 50% of members appointed as clinical experts in the management of diabetes. A majority vote was sufficient for a draft recommendation to be accepted. Each vote concluded with a Committee discussion on the vote results in which members were given an opportunity to discuss factors behind their individual votes. Draft recommendations could be modified by CERC during their deliberations.

Draft recommendations and GRADE Summary of Findings tables containing both the clinical and cost/cost-effectiveness data are provided in Appendix B.

Which treatment strategy to use?

If there is strong evidence that one treatment strategy dominates the alternative strategies (that is, it is both more effective and less costly), clearly this strategy would be chosen. However, if one treatment strategy is more effective but also more costly, then the choice is less clear and a pharmacoeconomic analysis can be undertaken to determine and compare the cost-effectiveness of the alternatives.

Pharmacoeconomic evaluations are the systematic assessment and comparative analysis of the costs and consequences of competing alternative treatment strategies. The results of a pharmacoeconomic evaluation are expressed as the difference in costs of the alternative strategies (incremental costs) divided by the difference in health outcomes of the alternative strategies (incremental health outcomes). Evaluations can be conducted in the form of a cost-effectiveness analysis (CEA) or a cost utility analysis (CUA). In a CEA, the costs are measured in monetary units and the health outcome is measured in a natural or clinical unit. In a CUA, the costs are measured in monetary units and the health outcome is expressed in quality-adjusted life years (QALYs). A QALY is a measurement of health outcome that considers both quantity and quality of life.

5. Identification of underlying values and preferences for each recommendation

An important component of each draft optimal therapy recommendation is a clear statement underlying values and preferences that supported CERC's choice of one alternative over another. These statements reflect the values expressed by CERC during their assessment of the clinical and cost-effectiveness evidence. Where the clinical-effectiveness and cost-effectiveness evidence was deemed insufficient to evaluate differences between treatments, recommendations were formulated to reflect clinical opinion and standard of care. The values and preferences statements for each treatment option are provided as a guide for patients, clinicians, and decision-makers in selecting the most appropriate treatment alternative.

6. Appraisal of overall quality of evidence

CERC voted on the overall quality of clinical evidence available for each recommendation. Possible ratings were "high", "moderate", and "low". This rating was based on an assessment of evidence quality across all outcomes considered "important" or "critical" by CERC. Where evidence was lacking for such outcomes, an overall rating of "low" was more likely, regardless of the quality of evidence for outcomes reported in studies. For example, the overall quality of evidence could be rated "low" due to the lack of data on long-term complications of diabetes, even if there was high-quality evidence available regarding surrogate outcomes such as A1C.

7. Grading strength of recommendations

The final step in the GRADE methodology is assigning the strength of each recommendation as either "strong" or "weak". This rating is intended to convey the degree of confidence the committee has that adherence to the recommendation will result in the desired outcome.²⁴ As stipulated by the GRADE process, strength of recommendations is reflected by the use of the words "suggests" or "recommends" (i.e., for weak recommendations, "CERC suggests that..." and for strong recommendations, "CERC recommends that...").

According to the GRADE Working Group, the rating of strength has implications for how users interpret a recommendation.²⁴

A “strong” recommendation:

1. is likely to be followed by most well-informed patients.
2. is unlikely to require decision aids to elicit patient values and preferences.
3. can often be implemented as policy.

A “weak” recommendation:

1. is likely to be followed by the majority of well-informed patients; however, a significant minority would choose not to follow the recommendation.
2. requires careful consideration of patient values and preferences. Decision aids may be helpful in determining the course of action.
3. is likely to require debate and involvement of multiple stakeholders before policy can be determined.

A proposed rating of strength (i.e., either “strong” or “weak”) was assigned to each recommendation, and feedback was provided by CERC members regarding the level of their agreement with the ratings. To facilitate this process, a summary of all prior CERC deliberations for each recommendation was distributed to members. This summary contained: the recommendation (with vote results), rating of overall quality of evidence (with vote results), listing of values and preferences (with vote results), a statement regarding the weight given by the committee to the economic evidence, a summary of contextual information, and proposed strength of recommendation. The proposed strength for each recommendation was based on answering four questions put forward by the GRADE Working Group as points of consideration when evaluating recommendation strength:

1. Is the available evidence of lower quality?
2. Is there uncertainty regarding the balance of benefits versus harms and burdens?
3. Is there uncertainty or are there differences in values and preferences?
4. Is there uncertainty about whether the net benefits are worth the costs?

An affirmative answer to one or more of these questions resulted in downgrading of a recommendation to “weak”. Where recommendations were graded as weak, the rationale supporting CERC’s decision is provided with the recommendation.

8. Identification of research gaps

Where there was insufficient information upon which to produce optimal therapy recommendations, CERC identified “gaps” in research/knowledge. These primarily consisted of treatment comparisons and populations for which no peer-reviewed reports of randomized controlled trials or observational studies were identified. Research gaps were also identified when there was a paucity of comparative data on outcomes of interest for particular treatment comparisons or populations.

9. Consideration of stakeholder feedback and drafting of final optimal therapy recommendations

Stakeholder feedback will be elicited through a web-based process on a report containing draft optimal therapy recommendations, summaries of the available evidence, and research gaps. This feedback will be collated and provided to CERC for consideration prior to drafting of the final optimal therapy recommendations for blood glucose test strips.

APPENDIX D: Abbreviations

A1C	glycosylated hemoglobin
CERC	COMPUS Expert Review Committee
COMPUS	Canadian Optimal Medication Prescribing and Utilization Service
GRADE	Grades of Recommendations Assessment, Development, and Evaluation
ICUR	incremental cost utility ratio
QALY	quality adjusted life year
RCT	randomized controlled trial
RR	relative risk
SMBG	self-monitoring of blood glucose
WMD	weighted mean difference

APPENDIX E: Glossary

A1C: A glycosylated form of hemoglobin, formed by the attachment of sugars to the hemoglobin molecule when glucose levels are elevated. A1C levels increase with the average concentration of glucose in the blood.

Cohort study: A longitudinal observational study (prospective or retrospective) in which participants are selected according to exposure status (before the outcome is determined), followed over time and the outcomes for each group compared.

Confidence interval: The interval in which a population parameter lies, based on a random sample of the population. The most commonly reported confidence interval is the 95% confidence interval.

Cost-effectiveness analysis: A form of economic evaluation that compares the costs and effects of two or more alternative treatments.

Cross-over trial: A type of randomized controlled trial in which the intervention is applied at different times to each subject; that is, after a specified period of time the original experimental group becomes the control group, and the original control group becomes the experimental group.

Diabetes mellitus: A group of common metabolic disorders characterized by hyperglycemia

Effectiveness: The extent to which an intervention, procedure, regimen, or service produces the intended outcomes when deployed under routine (“real world”) circumstances.

Efficacy: The extent to which an intervention, procedure, regimen, or service produces a beneficial outcome under ideal circumstances (e.g., in a randomized controlled trial).

Fasting plasma glucose: Plasma glucose level measured when there has been no caloric intake for at least 8 hours.

Gestational diabetes mellitus: Defined as glucose intolerance with first onset during pregnancy. It is usually a temporary condition.

Health-related quality of life: A broad theoretical construct developed to explain and organize measures concerned with the evaluation of health status, attitudes, values, and perceived levels of satisfaction and general well-being with respect to either specific health conditions or life as a whole from the individual perspective.

Heterogeneity (I^2): This statistic describes the degree of variation, as a percentage, between the results of individual studies within a meta-analysis.

Hyperglycemia: A qualitative term used to describe blood glucose that is above the normal range.

Hypoglycemia: A qualitative term used to describe blood glucose that is below the normal range and defined by 1) the development of autonomic or neuroglycopenic symptoms; 2) a low plasma glucose level of 4.0 mmol/l for patients with insulin or an insulin secretagogue; and 3) symptoms responding to the administration of carbohydrate (Canadian Diabetes Association 2003).

Incremental cost-utility ratio: Ratio of the difference in costs between an intervention and comparator, to the difference in effects measured in quality-adjusted life-years.

Large for gestational age: Births weight equal to or greater than the 90th percentile for a given gestational age.

Macrosomia: usually defined as a birth weight greater than 4.0 kg or 4.5 kg

Meta-analysis: Statistical synthesis of the results of individual studies that examine the same question to produce a single estimate of effect.

Monogenic diabetes: Rare forms of diabetes that result from mutations in a single gene. Most such mutations reduce the body's ability to produce insulin. Neonatal diabetes mellitus and maturity-onset diabetes of the young (MODY) are the two main forms of monogenic diabetes.

Nocturnal hypoglycemia: Hypoglycemic events that occur at night, usually from 24:00 h to 6:00 h.

Overall hypoglycemia: Overall hypoglycemia is defined by either symptoms or signs of hypoglycaemia and/or blood glucose < 4 mmol/L.

Quality adjusted life year (QALY): A health outcome measure that combines both quantity (mortality) and quality of life (morbidity). This measure enables comparisons across diseases and programs.

Randomized controlled trial: A prospective experimental study designed to test the efficacy of an intervention in which patients are randomly allocated to either a treatment group or the control group.

Rate ratio: The ratio of the person-time incidence rate in the exposed group to the person-time incidence rate in the unexposed group in an epidemiological study.

Relative risk: The ratio of the absolute risk of a disease among the exposed group to the absolute risk of the disease among the unexposed group in an epidemiological study.

Severe hypoglycemia: An event with characteristic hypoglycemic symptoms requiring assistance of another person.

Small for gestational age: Generally defined as the birth weight less than the 90th percentile for a given gestational age.

Standard deviation: A measure of the variability or spread of the data.

Systematic review: A summary of the medical literature that uses explicit methods to identify, select, appraise, and analyze studies relevant to a particular clinical question.

Type 1 diabetes mellitus: Diabetes that is primarily the result of pancreatic beta cell destruction due to an autoimmune process or for which the etiology of beta cell destruction is unknown.

Type 2 diabetes mellitus: It may range from predominant insulin resistance with relative insulin deficiency to a predominant secretory defect with insulin resistance.

Utility: A quantitative expression of an individual's preference for a particular health state.

References

1. Schütt M, Kern W, Krause U, Busch P, Dapp A, Grziwotz R, et al. Is the frequency of self-monitoring of blood glucose related to long-term metabolic control? Multicenter analysis including 24,500 patients from 191 centers in Germany and Austria. *Exp Clin Endocrinol Diabetes* 2006;114(7):384-8.
2. Coster S, Gulliford MC, Seed PT, Powrie JK, Swaminathan R. Monitoring blood glucose control in diabetes mellitus: a systematic review. *Health Technol Assess (Winch Eng)* [Internet] 2000;4(12). Available: <http://www.hta.nhs.uk/execsumm/summ412.shtml> (accessed 2009 Feb 23).
3. Davidson MB. Counterpoint. Self-monitoring of blood glucose in type 2 diabetic patients not receiving insulin: a waste of money [letter]. *Diabetes Care* [Internet] 2005;28(6):1531-3. Available: <http://care.diabetesjournals.org/cgi/content/full/28/6/1531> (accessed 2009 Feb 23).
4. Davidson MB, Castellanos M, Kain D, Duran P. The effect of self monitoring of blood glucose concentrations on glycated hemoglobin levels in diabetic patients not taking insulin: a blinded, randomized trial. *Am J Med* 2005;118(4):422-5.
5. *2005/06 report card for the Ontario drug benefit program* [Internet]. Toronto: Ministry of Health and Long-Term Care; 2006. Available: http://www.health.gov.on.ca/english/public/pub/ministry_reports/odb_report05/drug_rep.html (accessed 2008 Jun 23).
6. *2004/05 report card for the Ontario drug benefit program* [Internet]. Toronto: Ministry of Health and Long-Term Care; 2005. Available: http://www.health.gov.on.ca/english/public/pub/ministry_reports/odb_report04/drug_rep.html (accessed 2008 Jun 23).
7. *2003/04 report card for the Ontario drug benefit program* [Internet]. Toronto: Ministry of Health and Long-Term Care; 2004. Available: http://www.health.gov.on.ca/english/public/pub/ministry_reports/odb_report03/drug_rep.html (accessed 2008 Jun 23).
8. *Diabetes in Canada: highlights from the National Diabetes Surveillance System 2004-2005* [Internet]. Ottawa: Public Health Agency of Canada; 2008. Available: <http://www.phac-aspc.gc.ca/publicat/2008/dicndss-dacsnsd-04-05/pdf/dicndss-04-05-eng.pdf> (accessed 2008 Jun 26).

9. *Utilization of oral antiglycemics in Canada*. [unpublished dataset]. Ottawa (ON): Brogan, Inc.; 2008.
10. Canadian Agency for Drugs and Technologies in Health. Current utilization on blood glucose test strips in Canada. *Optimal Therapy Report - COMPUS* [Internet] 2009;3(4). Available: http://www.cadth.ca/media/pdf/compus_CU_Report-BGTS.pdf (accessed 2009 Mar 31).
11. *Diabetes: facts & figures* [Internet]. Ottawa: Public Health Agency of Canada; 2008. Available: http://www.phac-aspc.gc.ca/publicat/2008/ndfs-fnrd-08/ndfs_ff-fnrd_fc-eng.php (accessed 2009 Mar 20).
12. *Diabetes in Canada* [Internet]. 2nd edition. Ottawa: Health Canada; 2002. Available: http://www.phac-aspc.gc.ca/publicat/dic-dac2/pdf/dic-dac2_en.pdf (accessed 2009 Mar 20).
13. UK Prospective Diabetes Study (UKPDS) Group. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes. *Lancet* 1998;352(9131):837-53.
14. The Diabetes Control and Complications Trial Research Group. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. *N Engl J Med* 1993;329(14):977-86.
15. *The prevalence and costs of diabetes* [Internet]. Toronto: Canadian Diabetes Association; 2007. Pub no. 114007 06-295 06/06 Q-50M. Available: <http://www.diabetes.ca/Files/prevalence-and-costs.pdf> (accessed 2009 Mar 20).
16. *Report from the national diabetes surveillance system: diabetes in Canada, 2008* [Internet]. Ottawa: Public Health Agency of Canada; 2008. Available: <http://www.phac-aspc.gc.ca/publicat/2008/ndssdic-snsddac-08/index-eng.php> (accessed 2009 Jan 23).
17. Canadian Diabetes Association 2008 clinical practice guidelines for the prevention and management of diabetes in Canada. *Can J Diabetes* [Internet] 2008;32(suppl 1):i-S201. Available: <http://www.diabetes.ca/files/cpg2008/cpg-2008.pdf> (accessed 2009 Mar 20).
18. Dawson KG, Gomes D, Gerstein H, Blanchard JF, Kahler KH. The economic cost of diabetes in Canada, 1998. *Diabetes Care* [Internet] 2002;25(8):1303-7. Available: <http://care.diabetesjournals.org/cgi/reprint/25/8/1303.pdf> (accessed 2009 Mar 20).
19. Institute of Health Economics. Consensus statement on self-monitoring in diabetes. *Consensus Statements* [Internet] 2006;1(1). Available: http://www.ihe.ca/documents/consensus_statement_complete_nov17_0.pdf (accessed 2009 Jan 9).
20. Benjamin EM. Self-monitoring of blood glucose: the basics. *Clin Diabetes* [Internet] 2002;20(1):45-7. Available: <http://clinical.diabetesjournals.org/cgi/reprint/20/1/45> (accessed 2008 Jan 23).

21. *The GRADE working group* [Internet]. [place unknown: publisher unknown]; 2008. Available: <http://www.gradeworkinggroup.org/index.htm> (accessed 2008 Oct 16).
22. Atkins D, Best D, Briss PA, Eccles M, Falck-Ytter Y, Flottorp S, et al. Grading quality of evidence and strength of recommendations. *BMJ* 2004;328(7454):1490.
23. Schunemann HJ, Hill SR, Kakad M, Bellamy R, Uyeki TM, Hayden FG, et al. WHO rapid advice guidelines on pharmacological management of humans infected with avian influenza A (H5N1) virus. *Lancet Infect Dis* 2007;7(1):21-31.
24. Schunemann HJ, Jaeschke R, Cook DJ, Bria WF, El-Solh AA, Ernst A, et al. An official ATS statement: grading the quality of evidence and strength of recommendations in ATS guidelines and recommendations. *Am J Respir Crit Care Med* 2006;174(5):605-14.
25. Lasserre MN, Johnson KR, Boers M, Tugwell P, Brooks P, Simon L, et al. Definitions and validation criteria for biomarkers and surrogate endpoints: development and testing of a quantitative hierarchical levels of evidence schema. *J Rheumatol* 2007;34(3):607-15.
26. Canadian Agency for Drugs and Technologies in Health. Optimal therapy recommendations for the prescribing and use of insulin analogues. *Optimal Therapy Report - COMPUS* [Internet] 2009;2(7). Available: http://www.cadth.ca/media/pdf/compus_IA_OT_rec_report.pdf (accessed 2009 Mar 27).
27. Rohlfing CL, Wiedmeyer HM, Little RR, England JD, Tennill A, Goldstein DE. Defining the relationship between plasma glucose and HbA_{1c}: analysis of glucose profiles and HbA_{1c} in the Diabetes Control and Complications Trial. *Diabetes Care* [Internet] 2002;25(2):275-8. Available: <http://care.diabetesjournals.org/cgi/reprint/25/2/275> (accessed 2009 Mar 27).
28. Larsen ML. The clinical usefulness of glucated haemoglobin in diabetes care evaluated by use of a medical technology assessment strategy. *Dan Med Bull* 1997;44(3):303-15.
29. Goldstein DE, Little RR, Lorenz RA, Malone JI, Nathan DM, Peterson CM. Tests of glycemia in diabetes. *Diabetes Care* [Internet] 2004;27(7):1761-73. Available: <http://care.diabetesjournals.org/cgi/content/full/27/7/1761> (accessed 2009 Mar 27).
30. Canadian Diabetes Association 2003 clinical practice guidelines for the prevention and management of diabetes in Canada. *Can J Diabetes* 2003;27(Suppl 2):i-S140.
31. Diabetes Control and Complications Trial Research Group. Effect of intensive therapy on the microvascular complications of type 1 diabetes mellitus. *JAMA* 2002;287(19):2563-9.
32. Gerstein HC. Glycosylated hemoglobin: finally ready for prime time as a cardiovascular risk factor. *Ann Intern Med* [Internet] 2004;141(6):475-6. Available: <http://www.annals.org/cgi/reprint/141/6/475.pdf> (accessed 2009 Mar 27).
33. Khaw KT, Wareham N, Bingham S, Luben R, Welch A, Day N. Association of hemoglobin A_{1c} with cardiovascular disease and mortality in adults: the European

- prospective investigation into cancer in Norfolk. *Ann Intern Med* [Internet] 2004;141(6):413-20. Available: <http://www.annals.org/cgi/reprint/141/6/413.pdf> (accessed 2009 Mar 27).
34. Clarke PM, Gray AM, Briggs A, Farmer AJ, Fenn P, Stevens RJ, et al. A model to estimate the lifetime health outcomes of patients with type 2 diabetes: the United Kingdom Prospective Diabetes Study (UKPDS) Outcomes Model (UKPDS no. 68). *Diabetologia* 2004;47(10):1747-59.
 35. Selvin E, Marinopoulos S, Berkenblit G, Rami T, Brancati FL, Powe NR, et al. Meta-analysis: glycosylated hemoglobin and cardiovascular disease in diabetes mellitus. *Ann Intern Med* [Internet] 2004;141(6):421-31. Available: <http://www.annals.org/cgi/reprint/141/6/421.pdf> (accessed 2009 Mar 27).
 36. Reusch JE. Diabetes, microvascular complications, and cardiovascular complications: what is it about glucose? *J Clin Invest* [Internet] 2003;112(7):986-8. Available: <http://www.jci.org/cgi/reprint/112/7/986> (accessed 2009 Mar 27).
 37. Fleming TR, DeMets DL. Surrogate end points in clinical trials: are we being misled? *Ann Intern Med* 1996;125(7):605-13.
 38. Diabetes Control and Complications Trial Research Group. The relationship of glycemic exposure (HbA_{1c}) to the risk of development and progression of retinopathy in the diabetes control and complications trial. *Diabetes* 1995;44(8):968-83.
 39. Diabetes Control and Complications Trial Research Group. Effect of intensive diabetes treatment on the development and progression of long-term complications in adolescents with insulin-dependent diabetes mellitus: Diabetes Control and Complications Trial. *J Pediatr* 1994;125(2):177-88.
 40. UK Prospective Diabetes Study (UKPDS) Group. Effect of intensive blood-glucose control with metformin on complications in overweight patients with type 2 diabetes (UKPDS 34). *Lancet* 1998;352(9131):854-65.
 41. Ewart RM. The case against aggressive treatment of type 2 diabetes: critique of the UK prospective diabetes study. *BMJ* 2001;323(7317):854-8.
 42. Stratton IM, Adler AI, Neil HA, Matthews DR, Manley SE, Cull CA, et al. Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study. *BMJ* 2000;321(7258):405-12.
 43. Rosen CJ. The rosiglitazone story--lessons from an FDA Advisory Committee meeting. *N Engl J Med* 2007;357(9):844-6.
 44. Richter B, Bandeira-Echtler E, Bergherhoff K, Clar C, Ebrahim SH. Rosiglitazone for type 2 diabetes mellitus. *Cochrane Database Syst Rev* 2007;(3):CD006063.

45. Kahn SE, Haffner SM, Heise MA, Herman WH, Holman RR, Jones NP, et al. Glycemic durability of rosiglitazone, metformin, or glyburide monotherapy. *N Engl J Med* [Internet] 2006;355(23):2427-43. Available: <http://content.nejm.org/cgi/reprint/355/23/2427.pdf> (accessed 2009 Mar 27).
46. Nissen SE, Wolski K. Effect of rosiglitazone on the risk of myocardial infarction and death from cardiovascular causes. *N Engl J Med* 2007;356(24):2457-71.
47. Oiknine R, Bernbaum M, Mooradian AD. A critical appraisal of the role of insulin analogues in the management of diabetes mellitus. *Drugs* 2005;65(3):325-40.
48. Ohkubo Y, Kishikawa H, Araki E, Miyata T, Isami S, Motoyoshi S, et al. Intensive insulin therapy prevents the progression of diabetic microvascular complications in Japanese patients with non-insulin-dependent diabetes mellitus: a randomized prospective 6-year study. *Diabetes Res Clin Pract* 1995;28(2):103-17.
49. Bowker SL, Majumdar SR, Johnson JA. Systematic review of indicators and measurements used in controlled studies of quality improvement for type-2 diabetes. *Can J Diabetes* [Internet] 2005;29(3):230-8. Available: http://www.diabetes.ca/files/Johnson_Systematic_Review-pages%20230-238.pdf (accessed 2009 Mar 27).
50. A Canadian consensus for the standardized evaluation of quality improvement interventions in Type-2 diabetes: development of a quality indicator set. *Can J Diabetes* 2005;29(3):220-9.
51. *Pargluva™ Muraglitazar (BMS-298585)* [Internet]. Advisory Committee Briefing Document. Rockville (MD): U.S. Food and Drug Agency; 2005. Available: http://www.fda.gov/ohrms/dockets/ac/05/briefing/2005-4169B2_01_01-BMS-Pargluva.pdf (accessed 2009 Mar 27).
52. Norris SL, Lau J, Smith SJ, Schmid CH, Engelgau MM. Self-management education for adults with type 2 diabetes: a meta-analysis of the effect on glycemic control. *Diabetes Care* [Internet] 2002;25(7):1159-71. Available: <http://care.diabetesjournals.org/cgi/content/full/25/7/1159> (accessed 2009 Mar 27).
53. Chodosh J, Morton SC, Mojica W, Maglione M, Suttrop MJ, Hilton L, et al. Meta-analysis: chronic disease self-management programs for older adults. *Ann Intern Med* 2005;143(6):427-38.
54. Steed L, Cooke D, Newman S. A systematic review of psychosocial outcomes following education, self-management and psychological interventions in diabetes mellitus. *Patient Educ Couns* 2003;51(1):5-15.
55. Deakin T, McShane CE, Cade JE, Williams RD. Group based training for self-management strategies in people with type 2 diabetes mellitus. *Cochrane Database Syst Rev* 2005;(2):CD003417.

56. Ellis SE, Speroff T, Dittus RS, Brown A, Pichert JW, Elasy TA. Diabetes patient education: a meta-analysis and meta-regression. *Patient Educ Couns* 2004;52(1):97-105.
57. Oleckno WA. *Essential epidemiology: principles and applications*. Long Grove (IL): Waveland Press; 2002.
58. Canadian Agency for Drugs and Technologies in Health. *Systematic review of use of blood glucose test strips for the management of diabetes mellitus* [draft on the Internet]. Ottawa: The Agency; 2008. Available: http://www.cadth.ca/media/pdf/compus_Draft_BGTS_SR_report_of_clinical_outcome.pdf (accessed 2009 Feb 13).
59. Canadian Agency for Drugs and Technologies in Health. *Cost-effectiveness of blood glucose test strips in the management of adult patients with diabetes* [draft on the Internet]. Ottawa: The Agency; 2009. Available: http://www.cadth.ca/media/pdf/compus_Draft_BGTS_Consolidated_Econ_Report.pdf (accessed 2009 Feb 13).
60. Karter AJ, Ackerson LM, Darbinian JA, D'Agostino RB, Ferrara A, Liu J, et al. Self-monitoring of blood glucose levels and glycemic control: the Northern California Kaiser Permanente Diabetes Registry. *Am J Med* 2001;111(1):1-9.
61. Gordon D, Semple CG, Paterson KR. Do different frequencies of self-monitoring of blood glucose influence control in type 1 diabetic patients? *Diabet Med* 1991;8(7):679-82.
62. Evans JM, Newton RW, Ruta DA, MacDonald TM, Stevenson RJ, Morris AD. Frequency of blood glucose monitoring in relation to glycaemic control: observational study with diabetes database. *BMJ* 1999;319(7202):83-6.
63. Santiprabhob J, Likitmaskul S, Kiattisakthavee P, Weerakulwattana P, Chaichanwattanakul K, Nakavachara P, et al. Glycemic control and the psychosocial benefits gained by patients with type 1 diabetes mellitus attending the diabetes camp. *Patient Educ Couns* 2008;73(1):60-6.
64. Aydin H, Deyneli O, Yavuz D, Tarçin O, Akalin S. Does the frequency of the self-monitoring of blood glucose influence glycemic control in type 2 diabetic patients? *Marmara Med J* [Internet] 2005;18(1):13-6. Available: http://www.marmaramedicaljournal.org/pdf/pdf_MMJ_350.pdf (accessed 2008 Apr 16).
65. Davis WA, Bruce DG, Davis TM. Does self-monitoring of blood glucose improve outcome in type 2 diabetes? The Fremantle Diabetes Study. *Diabetologia* 2007;50(3):510-5.
66. Secnik K, Yurgin N, Lage MJ. Patterns of blood glucose monitoring in relation to glycemic control among patients with type 2 diabetes in the UK. *J Diabetes Complicat* 2007;21(3):181-6.
67. Barnett AH, Krentz AJ, Strojek K, Sieradzki J, Azizi F, Embong M, et al. The efficacy of self-monitoring of blood glucose in the management of patients with type 2 diabetes treated

- with a gliclazide modified release-based regimen. A multicentre, randomized, parallel-group, 6-month evaluation (DINAMIC 1 study). *Diabetes, Obesity & Metabolism* 2008;10(12):1239-47.
68. Guerci B, Drouin P, Grangé V, Bougnères P, Fontaine P, Kerlan V, et al. Self-monitoring of blood glucose significantly improves metabolic control in patients with type 2 diabetes mellitus: the Auto-Surveillance Intervention Active (ASIA) study. *Diabetes Metab* 2003;29(6):587-94.
 69. O'Kane MJ, Bunting B, Copeland M, Coates VE. Efficacy of self monitoring of blood glucose in patients with newly diagnosed type 2 diabetes (ESMON study): randomised controlled trial. *BMJ* 2008;336(7654):1174-7.
 70. Schwedes U, Siebolds M, Mertes G, SMBG Study Group. Meal-related structured self-monitoring of blood glucose: effect on diabetes control in non-insulin-treated type 2 diabetic patients. *Diabetes Care* [Internet] 2002;25(11):1928-32. Available: <http://care.diabetesjournals.org/cgi/reprint/25/11/1928> (accessed 2009 Mar 27).
 71. Farmer A, Wade A, Goyder E, Yudkin P, French D, Craven A, et al. Impact of self monitoring of blood glucose in the management of patients with non-insulin treated diabetes: open parallel group randomised trial. *BMJ* 2007;335(7611):132.
 72. Muchmore DB, Springer J, Miller M. Self-monitoring of blood glucose in overweight type 2 diabetic patients. *Acta Diabetol* 1994;31(4):215-9.
 73. Rindone JP, Austin M, Luchesi J. Effect of home blood glucose monitoring on the management of patients with non-insulin dependent diabetes mellitus in the primary care setting. *Am J Manag Care* 1997;3(9):1335-8.
 74. Wen L, Parchman ML, Linn WD, Lee S. Association between self-monitoring of blood glucose and glycemic control in patients with type 2 diabetes mellitus. *Am J Health Syst Pharm* 2004;61(22):2401-5.
 75. French DP, Wade AN, Yudkin P, Neil AW, Kinmonth AL, Farmer AJ. Self-monitoring of blood glucose changed non-insulin treated type 2 diabetes patients' beliefs about diabetes and self-monitoring in a randomised trial. *Diabet Med* 2008;25(10):1218-28.
 76. Siebolds M, Gaedeke O, Schwedes U, SMBG Study Group. Self-monitoring of blood glucose--psychological aspects relevant to changes in HbA1c in type 2 diabetic patients treated with diet or diet plus oral antidiabetic medication. *Patient Educ Couns* 2006;62(1):104-10.
 77. Simon J, Gray A, Clarke P, Wade A, Neil A, Farmer A. Cost effectiveness of self monitoring of blood glucose in patients with non-insulin treated type 2 diabetes: economic evaluation of data from the DiGEM trial. *BMJ* [Internet] 2008;336(7654):1177-80. Available: <http://www.bmj.com/cgi/reprint/336/7654/1177> (accessed 2009 Apr 1).

78. Martin S, Schneider B, Heinemann L, Lodwig V, Kurth HJ, Kolb H, et al. Self-monitoring of blood glucose in type 2 diabetes and long-term outcome: an epidemiological cohort study. *Diabetologia* 2006;49(2):271-8.
79. Scherbaum WA, Ohmann C, Abholz HH, Dragano N, Lankisch M. Effect of the frequency of self-monitoring blood glucose in patients with type 2 diabetes treated with oral antidiabetic drugs-a multi-centre, randomized controlled trial. *PLoS ONE* 2008;3(8):e3087.
80. Wieland LD, Vigil JM, Hoffman RM, Janis LW. Relationship between home glucose testing and hemoglobin A_{1c} in type II diabetes patients. *Am J Health Syst Pharm* 1997;54(9):1062-5.
81. Karter AJ, Parker MM, Moffet HH, Spence MM, Chan J, Ettner SL, et al. Longitudinal study of new and prevalent use of self-monitoring of blood glucose. *Diabetes Care* [Internet] 2006;29(8):1757-63. Available: <http://care.diabetesjournals.org/cgi/reprint/29/8/1757> (accessed 2009 Mar 13).
82. Murata GH, Duckworth WC, Shah JH, Wendel CS, Mohler MJ, Hoffman RM. Blood glucose monitoring is associated with better glycemic control in type 2 diabetes: a database study. *J Gen Intern Med* 2009;24(1):48-52.
83. Homko CJ, Sivan E, Reece EA. The impact of self-monitoring of blood glucose on self-efficacy and pregnancy outcomes in women with diet-controlled gestational diabetes. *Diabetes Educ* 2002;28(3):435-43.
84. Rey E. Usefulness of a breakfast test in the management of women with gestational diabetes. *Obstet Gynecol* 1997;89(6):981-8.