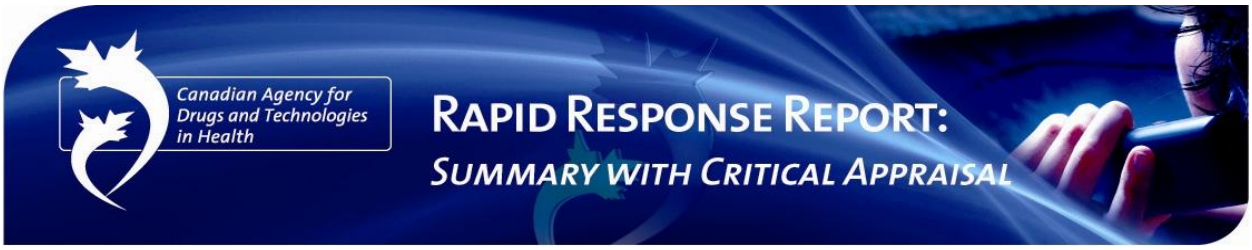

TITLE: Blood Glucose Monitors and Test Strips: A Review of the Comparative Clinical Evidence and Cost-Effectiveness – An Update

DATE: 15 March 2013

CONTEXT AND POLICY ISSUES

Blood glucose monitors measure blood glucose concentration using a drop of venous, arterial or, mainly, capillary blood from a finger puncture. Self-monitoring of blood glucose is recognized as one approach to improve glycemic control and reduce hypoglycemic events by alerting patients with diabetes to modify their hypoglycemic drug dose, diet, and physical activities.[2] Several different blood glucose monitors are available in Canada, and are listed in the appendices of this report. The total Canadian expenditure on blood glucose test strips in 2006 was an estimated $370 million,[3] and exceeded $500 million in 2010.[4] Although these devices were introduced three decades ago,[5] the accuracy obtained from available blood glucose monitors and test strips remains uncertain.[6] Furthermore, the introduction of new and relatively cheap test strips raises questions about the comparative cost-effectiveness of the available blood glucose monitors and test strips.[7]

This report will update a previous review produced by CADTH[8] that examined the clinical and cost-effectiveness of blood glucose monitors and test strips available in Canada.

RESEARCH QUESTIONS

1. What is the comparative clinical effectiveness of the available blood glucose monitors and test strips in Canada for patients with diabetes?

2. What factors in blood glucose monitors and test strips are related to better patient outcomes?

3. What are the most cost-effective models of blood glucose monitors and test strips for patients with diabetes?

KEY FINDINGS

Several blood glucose monitors are available in Canada. Comparative studies of five of these monitors were identified and the devices were shown to be clinically accurate. No evidence on the cost-effectiveness of blood glucose monitors and test strips for patients with diabetes was found.

METHODS

Literature Search Strategy

A limited literature search was conducted on key resources including PubMed, The Cochrane Library (2013, Issue 1), University of York Centre for Reviews and Dissemination (CRD), ECRI, MDALL databases, Canadian and major international health technology agencies, as well as a focused Internet search. No filters were applied to limit the retrieval by study type. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 2008 and February 15, 2013.

A list of the available SMBG devices in Canada is presented in APPENDIX 1.

Selection Criteria and Methods

One reviewer screened citations and selected studies. The first level of screening was based on the titles and abstracts of the identified citations. Full texts of any relevant titles/abstracts were retrieved, and the final article selection was based on the inclusion criteria presented in **Table 1**.

Table 1: Selection Criteria

Population	Patients with any type of diabetes (type I, type II, gestational)
Intervention	Blood glucose monitors and test strips systems available in Canada
Comparator	Blood glucose monitors and test strips systems available in Canada
Outcomes	Blood glucose measurements Hemoglobin A1C level Patient adverse events
Study Designs	Health technology assessments, systematic reviews, meta-analysis, randomized-controlled trials, non-randomized studies, and economic evaluations

Exclusion Criteria

Studies were excluded if they did not meet the selection criteria. Duplicate reports of the same outcomes from the same trials were also excluded. With regard to study population, studies were excluded if SMBG devices were evaluated among non-diabetic patients. Studies were also excluded if they evaluated SMBGs not available in Canada, or if they were evaluated after laboratory manipulation of blood samples, or when measurements were not done by patients or health care providers (i.e. laboratory evaluation only). Studies evaluating continuous and subcutaneous blood glucose monitors were also excluded. Finally, studies were excluded if they

did not directly compare different SMBGs, and if they evaluated the disease and patient management based on SMBGs when these evaluations did not provide direct comparisons between different SMBGs.

Critical Appraisal of Individual Studies

The quality appraisal of the included studies was assessed using a modified Quality Assessment of Diagnostic Accuracy Studies (QUADAS) checklist for diagnostic studies.[9] The modifications were introduced to reflect methodological components related to the evaluation of blood glucose monitors according to recommendations from the Clinical and Laboratory Standard Institute (CLSI).[10] APPENDIX 2 presents the modified QUADAS checklist.

For the included studies a numeric score was not calculated. Instead, the strengths and limitations of the study were described narratively.

SUMMARY OF EVIDENCE

Quantity of Research Available

A total of 455 potential citations were identified by the search in bibliographic database, with 414 citations being excluded during the title and abstract screening based on irrelevance to the questions of interest. The full text documents of the remaining 41 articles were retrieved. Of these 39 did not meet the inclusion criteria and were excluded,[1,11-48] leaving two articles that reported from two unique trials to be included in this review.[49,50] The literature search did not identify any comparative cost-effectiveness evaluations or studies on factors related to the SMBG devices that could affect patient outcomes. A PRISMA diagram demonstrating the study selection process is presented in APPENDIX 3.

Additional references of potential interest that did not meet inclusion criteria are provided in APPENDIX 4.

Summary of Study Characteristics

Two studies that partially addressed the comparative effectiveness question were included in this report. The accuracy and reliability of different SMBG devices were evaluated and compared in the included studies.[49,50] These studies did not evaluate or compare patient outcomes based on the SMBG device they used. Details regarding primary studies characteristics are tabulated in APPENDIX 5.

In a study funded by Abbott Diabetes care, Tack et al.[50] compared the accuracy of five SMBG devices. These included FreeStyle Lite (Abbott), FreeDom Lite (Abbott), Accu-Check Aviva (Roche), Contour (Bayer), and OneTouch UltraEasy (LifeScan); the reference test used was the YSI 2300 glucose analyzer. A total of 501 patients, with diabetes type I (49%) or type II (51%), were randomized to use three of the five evaluated devices to test the levels of blood glucose with, and all the SMBG measurements were carried out by the patients themselves.

The study by Zueger et al.[49] evaluated and compared the accuracy of three SMBG devices including FreeStyle Lite (Abbott), Accu-Check Aviva (Roche), and Contour (Bayer). The reference method was HemoCue Glucose 201+ System (point of care blood glucose measuring

device). One health care provider conducted the blood glucose measurements for the 150 patients included in the study.
In Both studies, patients who had severe hyperglycemia (≥ 75 mg/dl) were represented more than patients with milder blood glucose (< 75 mg/dl); 84% vs 14% in Tack's study[50] and 91% vs. 9% in Zueger's study.[49] Patients with severe diabetes are more likely to use the SMBGs than those with a less severe condition; therefore the trial population is representative of the type of patients who will use the device. However, the diagnostic accuracy and clinical efficacy of these devices when used by the less severe patients may by uncertain based on the included studies.

Both studies evaluated the accuracy of the SMBG devices based on the difference with the reference test. These differences were expressed in terms of mean bias, mean absolute relative difference, compliance with ISO 15197 (2003) and performance on the error grids. APPENDIX 6 briefly describes the accuracy criteria for ISO15197 and the Clark and Parkes error grids.

Summary of Critical Appraisal

The strength and limitations of included studies are summarized in APPENDIX 7.

In diagnostic studies, the use of a standardized, well established and widely accepted reference test is essential. This reference test gives the true classification of the tested participants as having the disease or not; this classification is necessary to estimate the accuracy of the new (index) test. Tack et al.[50] used the YSI 2300 glucose analyzer; this test is accepted by regulators for the validation of new SMBG devices. However, Zueger et al. conducted the reference testing with a point of care blood glucose tester.[49] The validity of these two tests as reference standards was not evaluated in this review.

The reproducibility of the diagnostic test should be evaluated by measuring the correlation or the difference between the results of the same test conducted on the same patients within a reasonable interval of time. Neither of the included studies evaluated the reproducibility of the SMBG devices. Nevertheless, both trials conducted the index and reference tests within reasonable time (within one hour) from each other; this would reduce the effect of blood glucose variations.

Interpretation of the index test results should be conducted without knowledge (blinded) of the reference test results. Awareness of the reference test outcomes might introduce a bias due to preconceived ideas. Both studies failed to use, or at least report, blinding of the reference test. This bias might be exaggerated by the fact that several index tests were used; therefore, knowing the results of some devices might affect the reading for the other devices. On the other hand, digital recording of the results may minimize this risk of bias; however, the method used for recording the results was not specified in the included trials.

In the study by Tack et al.,[50] it was noticed that 48 patients were enrolled but excluded from the analysis. The study publication did not report which group these excluded patients were in during the trial. However, the FreeStyle Lite and FreeDom Lite groups had fewer patients than the other groups. This may raise suspicion that there was selective exclusion of some patients which lead to the better performance estimates for these two devices.

Summary of Findings

A summary of study findings and authors' conclusions are provided in APPENDIX 8.

Mean Bias

The mean bias estimates the difference between the individual SMBG device and the reference test. Tack et al.[50] reported the following mean bias, from the lowest to the greatest: 0.3 mg/dl, 0.8 mg/dl, -1.2 mg/dl, 6.3 mg/dl and 7.2 mg/dl respectively for FreeDom Lite, FreeStyle Lite, Contour, OneTouch UltraEasy and Accu-Check Aviva.

Zueger et al.[49] reported different estimates and relative classification of the devices based on the mean bias. They reported mean bias of -2.7 mg/dl for Accu-Check Aviva, -6.3 mg/dl for FreeStyle Lite and -13.2 mg/dl for Contour.

The difference in magnitude between the two studies might be explained by the different reference tests used in the two trials. However, both studies had in common that the Contour SMBG had the largest negative mean bias; this might indicate that this device has tendency to give blood glucose readings below the real values. The potential impact is that episodes of hyperglycemia may be misdiagnosed as normal.

The differences between devices in terms of the mean bias were estimated in both trials. Tack et al.[50] showed that the difference in mean bias between FreeStyle Lite and FreeDom Lite, FreeDom Lite and Accu-Check Aviva, and Contour and OneTouch UltraEasy were not statistically significant. In contrast, Zueger et al.[49] reported that the difference in mean bias between FreeStyle Lite and Accu-Check Aviva was not statistically significant. All other comparisons were statistically significant in both studies.

Mean absolute relative difference (MARD)

MARD is a continuous measure that uses the magnitude of the relative difference for each observation, and it estimates the accuracy of the device. The results of MARD are expressed in percentage; the lower percentage indicates better accuracy performance. Tack et al.[50] reported that FreeStyle Lite and FreeDom Lite had the lowest MARD estimates, while Contour and OneTouch UltraEasy had the highest MARD. Zueger et al.[49] showed that Contour device had the highest MARD estimate, and Accu-Check and FreeStyle Lite had lower estimates.

Performance of the SMBG devices on Error Grids

The Clarke Error Grid was used in both trials, and it was shown that all evaluated devices had ≥90% of the tested samples in zone A of the grid; zone A indicates that index test produces accurate results. More specifically, FreeStyle Lite, FreeDom Lite and Accu-Check all had ≥96% of samples in zone A in both studies.[49,50] Contour device had between 92% and 94% of the measured samples in zone A,[49,50] while OneTouch UltraEasy scored the lowest percentage of 90.4% of the samples in the zone A.

Limitations

This review was based on information available in the published scientific literature which may not provide evidence for all available SMBG devices. This fact might introduce a publication bias on the results presented in the report. The literature search strategy, however, included grey literature (publication from non-traditional sources), reducing the risk of publication bias. Another

limitation is the lack of comparative cost-effectiveness evaluations between the different blood glucose monitors and test strips, for this reason a conclusion on their cost-effectiveness cannot be drawn. Furthermore, our literature search and study selection was based on blood glucose monitors available in Canada, so the generalizability and external validity of this report to all SMBG monitors and test strips should be evaluated within the scope of the review, and within the limitations of the included studies.

CONCLUSIONS AND IMPLICATIONS FOR DECISION OR POLICY MAKING

This report had the objective of updating a previous rapid response review about the comparative effectiveness and cost-effectiveness of SMBG devices available in Canada. In the previous review, the comparative effectiveness of the evaluated SMBGs, in terms of diagnostic accuracy, could not be evaluated. In this update however, the diagnostic accuracy and performance of five SMBG devices were reviewed and compared in this review. The available evidence showed that FreeStyle Lite, FreeDom Lite and Accu-Check Aviva SMBG devices may have better accuracy and performance that Contour and OneTouch UltraEasy devices. These findings must be interpreted with caution, given the limited scope of the review to blood glucose monitors available in Canada, and the included studies' limitations. No evidence on the most cost-effective models of blood glucose monitors and test strips for patients with diabetes was identified.

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APPENDIX 1. Listing of SMBGs Devices Available in Canada

List of SMBGs Devices Available in Canada not Included in the Original CADTH Review

Manufacturer	Meter System	Test Strip
Acon Laboratories	On-Call Plus	On-Call Plus
	On Call Advanced	On Call Advanced
Agamatrix	Keynote Blood Glucose Monitoring System	Keynote Blood Glucose Monitoring System - Test Strips
	Jazz Blood Glucose Monitoring System	Jazz Test Strips
	Agamatrix Blood Glucose Monitoring System	Agamatrix Test Strips
	Iagamatrix Blood Glucose Monitoring System	
Btnx Inc.	Rapid Response Blood Glucose Monitoring System - Meter	Rapid Response Blood Glucose Monitoring System - Test Strip
Animas	Onetouch Ping Glucose Management System – Meter And Insulin Pump	Compatible With Onetouch Ultra Blue Test Strips
Bionime Corporation	Rightest System – Gm 100 Meter	Rightest Test Strip
	Rightest System – Gm 300 Meter	
	Rightest System – Gm 550 Meter	
EPS Biotechnology	Easyplus Self-Monitoring Blood Glucose System - Meter	Easyplus Self-Monitoring Blood Glucose System - Test Strips
	Easyplus R13 System - Self-Monitoring Blood Glucose Meter	Easyplus R13 System - Test Strips
	Easyplus R13n Self-Monitoring Blood Glucose System - Meter	Easyplus R13n Self-Monitoring Blood Glucose System - Test Strips
	Easyplus V Self-Monitoring Blood Glucose System - Blood Glucose Meter	Easyplus V Self-Monitoring Blood Glucose System - Blood Glucose Test Strips
Ideal Life	Ideal Life Glucomanager	Glucose Test Strip
I-Sens	Bravo Blood Glucose Meter	Bravo Blood Glucose Test Strip
	Caresens N Blood Glucose Meter	Caresens N Blood Glucose Test Strip
Lernapharm (Loris) Inc. / Gluco Plus Inc.	Glucoplus Blood Glucose Complete Monitoring System	Glucose Plus 50 Test Strips
Major Biosystem Corporation	Ap-1001 Blood Glucose Monitoring System - Blood Glucose Meter	Ap-1001 Blood Glucose Monitoring System - Blood Glucose Test Strip
Medi+Sure Canada	Medi+Sure Blood Glucose System - Med+Sure Blood Glucose Meter	Medi+Sure Blood Glucose System - Medi+Sure Blood Glucose Test Strip
Nova Biomedical	Nova Max Link Blood Glucose Monitor	Nova Max Test Strips

List of SMBGs Devices Available in Canada not Included in the Original CADTH Review

Manufacturer	Meter System	Test Strip
Corporation	Nova Max Blood Glucose Monitor	
Sanofi-Aventis Canada	BG-Star Blood Glucose Monitoring System	Bgstar Blood Glucose Test Strips
	IBG-Star Blood Glucose Monitoring System	
Taidoc Technology Corporation	Fora D15b Blood Glucose Monitoring System	Fora D15b Blood Glucose Test Strip
	Fora D15c Blood Glucose Monitoring System	Fora D15c Blood Glucose Test Strip
	Fora D15z Blood Glucose Monitoring System	Fora D15z Blood Glucose Test Strip
	Fora D20 Blood Glucose Plus Blood Pressure Monitoring System	Fora D20 Blood Glucose Test Strip
	Clever Check - Glucose Meter	Clever Check - Glucose Test Strip
	Td-4244 Blood Glucose Monitoring System	Td-4244 Blood Glucose Test Strip
Tremblay Harrison	Ez Health Oracle Blood Glucose Meter	Ez Health Oracle Glucose Test Strips
	Ez Health Oracle Onyx Blood Glucose Meter	
	Ez Health Oracle Talking Blood Glucose Meter	
	Ez Health Autocode Blood Glucose Monitoring System - Meter	Ez Health Autocode Blood Glucose Monitoring System - Glucose Test Strips

List of SMBG Devices Available in Canada – Used for the Literature Search in the Original CADTH Review

Manufacturer, distributor contact information	Meter system	Test strips	Test strip expiration	Test strip package size availability*
Abbott Diabetes Care (888) 519-6890 (905) 542-8637 www.abbottdiabetescare.ca	G2 Sensor Care Blood Glucose Monitor This was available in 2006 but is no longer in circulation			
	Sof-Tact Sof-Tact meters and Sof-Tact test strips are no longer available.	The strips are called Sof-Tact electrodes strips	Expiration date printed on foil packet and box	□ 100s
	FreeStyle FreeDom Lite Blood Glucose Monitoring System	FreeStyle Lite	Until expiration on box	□ 50s □ 100s
	FreeStyle Lite Blood Glucose Monitoring System □ Previously known as *FreeStyle Mini* □ Same as *FreeDom* monitor except for addition of four programmable alarms			
	Precision Xtra Blood Glucose and Ketone Monitoring System (Replaces *PrecisionQID* and *Xtra* meters.)	Precision Xtra Blood β Ketone Test Strips	On foil packet and test strip box	
Auto Control Medical Inc. (800) 461-0991 www.autocontrol.com	iTest Blood Glucose Monitoring System	iTest	Until expiration on box or 90 days after opening the first vial.	□ 50s □ 100s
Bayer Healthcare (800) 268-7200 www.bayerdiabetes.ca	Bayer Ascensia Autodisc Bayer no longer makes these, though they are still being sold online but not by Bayer. They were for the older Ascensia DEX 2/DEX and can be used in Bayer's Breeze 2			□ 50s □ 100s
	Bayer Ascensia Microfill Bayer no longer makes this product. It is still sold online but not by Bayer. It was used for the Ascensia Contour Blood Glucose Meter that is now called Bayer Contour			□ 50s □ 100s
	Bayer's Breeze 2	Bayer's Breeze 2	Until expiration on box	□ Disc of 10
	Bayer's Contour	*Ascensia CONTOUR* Test	6 months after opening vial or by the	□ 50s □ 100s

List of SMBG Devices Available in Canada – Used for the Literature Search in the Original CADTH Review

Manufacturer, distributor contact information	Meter system	Test strips	Test strip expiration	Test strip package size availability*
		Strips	expiration date	
	Bayer's Contour Link (Same as *Contour*, except for additional wireless device for data transfer to software program)			(25s available in Quebec only.)
	Bayer Ascensia ELITE and ELITE XL have been discontinued. Supplies for these meters can be ordered.	Ascensia ELITE Blood Glucose Strips	On test strip foil or on the carton	□ 50s □ 100s
	NEW Bayer Contour USB	Bayer's CONTOUR test strips	Expiration date on bottle	□ 50s □ 100s
	NEW Bayer Diget	Bayer's CONTOUR test strips	Expiration date on bottle	□ 50s □ 100s
Lifescan Canada Ltd. (800) 663-5521 www.onetouch.ca	OneTouch Ultra2	OneTouch Ultra test strips with advanced *DoubleSure technology*	Until expiration on box or 6 months from opening the first vial	□ 50s □ 100s
	OneTouch UltraMini			
	OneTouch UltraSmart			
	InDuo System (Meter no longer available, but strips still sold.)	OneTouch Ultra	3 months after opening vial	
	OneTouch Ping (Designed for wireless communication with *Animas* insulin pump.)	OneTouch Ultra		
	OneTouch SureStep (Meter no longer available, but strips still sold.)	OneTouch SureStep		
	OneTouch Ultra (Meter no longer available, but strips still sold.)	OneTouch Ultra		

List of SMBG Devices Available in Canada – Used for the Literature Search in the Original CADTH Review

Manufacturer, distributor contact information	Meter system	Test strips	Test strip expiration	Test strip package size availability*
Roche Diagnostics (800) 363-7949 www.accu-chek.ca	Accu-Chek Aviva Nano	Accu-Chek Aviva	Until expiration on box	□ 50s □ 100s
	Accu-Chek Aviva			
	Accu-Chek Compact Plus (Replaces *Accu-Chek Compact All-in-One System*.)	Accu-Chek Compact (Pre-loaded drum with 17 test strips)	3 months after loading drum, meter prompts patient to change/replace drum. Also, the expiry date is printed on the pack and on the peel-off label on the drum container.	□ 51 (=3 drums of 17 strips) □ 102 (=6 drums of 17 strips)
	Accu-Chek Voicemate Plus (blood glucose monitor for the blind and visually impaired) □ Only available through Accu-Chek Customer Care: (800) 363-7949			
	Accu-Chek Advantage (Meter no longer available, but strips still sold.)	Accu-Chek Advantage Or Advantage Comfort Test Strip	Until expiration on box	□ 50s □ 100s
	Accusoft Advantage (Meter no longer available, but strips still sold.)			
	NEW Accu-Ckek Mobile	No strips but 50 strips on one cassette	Each cassette must be used within three months of putting it in the meter. Also the expiry date is shown on the box of the test cassette and on the lid film of the	□ 50s

List of SMBG Devices Available in Canada – Used for the Literature Search in the Original CADTH Review

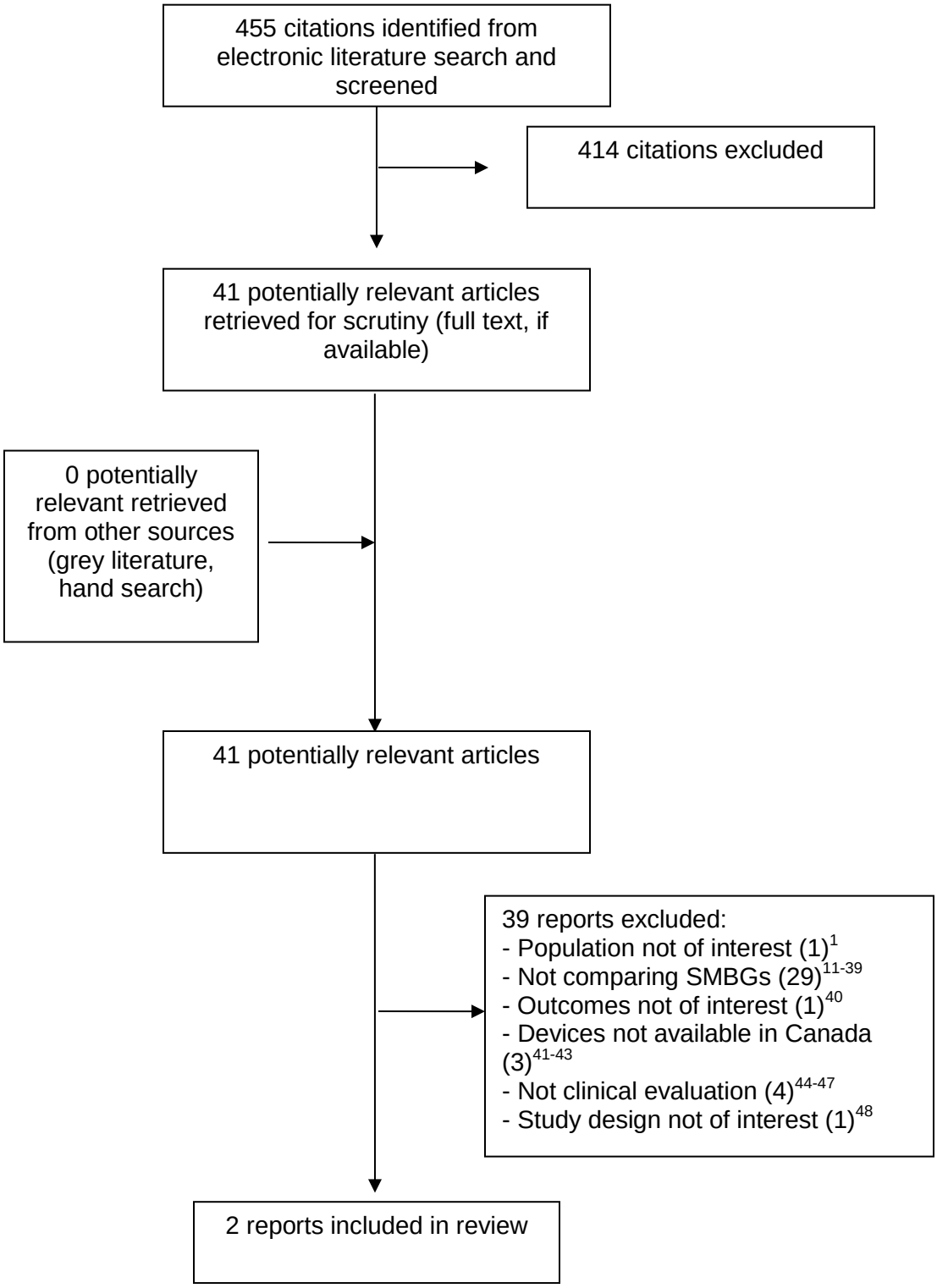
Manufacturer, distributor contact information	Meter system	Test strips	Test strip expiration	Test strip package size availability*
			foil-sealed packaging.	
Nova Biomedical (800) 260-1021 www.novacares.ca	NovaMax	NovaMax test strips	3 months after opening vial	□ 50s □ 100s
	NovaMax Link (Designed for wireless communication with *Medtronic insulin pump*.)			
	NEW NovaMaxPLUS			□ 50s □ 100s
EZHealth (866) 829-7926 www.oracledіabetes.com	Oracle	EZHealth Oracle test strips	3 months after opening vial	□ 50s □ 100s
Nipro Diagnostics Toll free: 1-800-803-6025 International: 1-954-677-4599 http://www.niprodiagnostics.com	TRUEtrack	TRUEtrack test strips	4 months after opening vial	□ 50s □ 100s
	Sidekick (All-in-one disposable meter-test strip system. Test strips cannot be purchased separately)	50 built-in test strips		□ 50s (built into meter; not sold separately)
	TRUEresult Meter	TRUEtest Strips	4 months after opening the vial or after expiry date written on the vial label.	□ 50s □ 100s
	TRUE2go	TRUEtest Strips		□ 50s □ 100s
*Company was contacted by phone if package size information not supplied on corporate website				

APPENDIX 2. Modified QUADAS Checklist[9]

Item	Yes	No	Unclear	NA
Population				
1. Was the spectrum of participants representative of the patients who will receive the test in practice?				
2. Were selection criteria clearly described?				
3. Were withdrawals from the study explained?				
Blood Sampling				
4. Was blood hematocrit checked to be within monitor's acceptable range?*				
5. Did the distribution of glucose in blood samples span monitor's measurement range?*				
6. Did the trial use appropriate anticoagulant, blood additives, or preservatives?*				
7. Was the catheter properly flushed of IV solution prior to sampling?*				
8. Was the skin cleaned and dried prior to puncture?*				
Index test (monitor)				
9. Was the execution of the Index monitor described in sufficient detail to permit its replication?				
10. Were operators** trained to manufacturer's instructions?*				
11. Was the Index monitor tested in duplicate?*				
Reference test				
12. Was the reference standard likely to classify the target condition correctly?				
13. Was the execution of the reference standard described in sufficient detail to permit its replication?				
14. Was the laboratory method checked for stability and for being within its QC control limits?*				
15. Was the laboratory method tested in duplicate?*				
16. Was the laboratory method is verified within NIST standard reference materials?*				
17. Were the laboratory duplicated within 4% or 0.22 mmol/L (4 mg/dL) (or else excluded)?*				
Verification				
18. Were both monitor and reference method tested from the same sample?*				
19. Was the period between performance of the reference standard and the index monitor short enough to be reasonably sure that the target condition did not change between the two tests?				
20. Was blood tested (or centrifuged) within 5 min of monitor test. Was the centrifuged plasma tested with reference method within 60 min of monitor test?*				
21. Did the whole sample or a random selection of the sample receive verification using the reference standard?				
22. Did participants receive the same reference standard regardless of the index test result?				
23. Was the reference standard independent of the index test? (that is, the index test did not form part of the reference standard)				
24. **Interpretation**				
25. Were the Index monitor results interpreted without knowledge of the results of the reference standard?				
26. Were the reference standards results interpreted without knowledge of the results of the index test?				
27. Were the same clinical data available when the test results were interpreted as would be available when the test is used in practice?				
28. Did the trial use standardized acceptance criteria?*				

***** Items adapted from the clinical and laboratory standard institute recommendations[10]
NA=Not applicable

APPENDIX 3. Selection of Included Studies



APPENDIX 4. Additional Studies of Potential Interest

Studies on devices not available in Canada

1. Ogawa T, Murakawa M, Matsuda A, Kanozawa K, Kato H, Hasegawa H, et al. Endogenous factors modified by hemodialysis may interfere with the accuracy of blood glucose-measuring device. Hemodial Int. 2012 Apr;16(2):266-73.

2. Chen CC, Lin JJ, Hung ST, Chun PT, Lai YK. The clinical performance of the EGV1 self-monitoring blood glucose system. Clin Chim Acta. 2012 Jul 11;413(13-14):1039-44.

3. Harman-Boehm I, Gal A, Raykhman AM, Zahn JD, Naidis E, Mayzel Y. Noninvasive glucose monitoring: a novel approach. J Diabetes Sci Technol. 2009 Mar [cited 2013 Feb 20];3(2):253-60. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2771521

Studies validating SMBGs without comparing them with other SMBGs devices

1. Pfutzner A, Mitri M, Musholt PB, Sachsenheimer D, Borchert M, Yap A, et al. Clinical assessment of the accuracy of blood glucose measurement devices. Curr Med Res Opin. 2012 Apr;28(4):525-31.

2. Baumstark A, Pleus S, Schmid C, Link M, Haug C, Freckmann G. Lot-to-lot variability of test strips and accuracy assessment of systems for self-monitoring of blood glucose according to ISO 15197. J Diabetes Sci Technol. 2012 Sep;6(5):1076-86.

3. Freckmann G, Schmid C, Baumstark A, Pleus S, Link M, Haug C. System accuracy evaluation of 43 blood glucose monitoring systems for self-monitoring of blood glucose according to DIN EN ISO 15197. J Diabetes Sci Technol. 2012 Sep;6(5):1060-75.

4. Dimeski G, Jones BW, Tilley V, Greenslade MN, Russell AW. Glucose meters: evaluation of the new formulation measuring strips from Roche (Accu-Chek) and Abbott (MediSense). Ann Clin Biochem. 2010 Jul;47(Pt 4):358-65.

APPENDIX 5. Characteristics of the Included Studies

Study Objectives and Design	Patient Characteristics	Intervention, Comparator, and Study Conduct	Clinical Outcomes
Tack et al. 2012[50] – Netherlands/ Germany			
To compare the mean absolute relative differences and the compliance with accuracy criteria between five SMBGs. Diagnostic Study The study was funded by Abbott Diabetes Care	○ Trial size: 501 patients ○ Diabetes ▪ type I (49.4%) ▪ type II (50.6%) ○ Age ▪ mean (SD): 53 (15) years ○ Male patients (57.6%)	○ Intervention (Index test) ▪ FreeStyle Lite FreeStyle (Abbott) ▪ FreeDom Lite (Abbott) ▪ Accu-Check Aviva (Roche) ▪ Contour (Bayer) ▪ OneTouch UltraEasy (LifeScan) ○ Comparator (Reference test) ▪ YSI 2300 glucose analyzer – glucose oxidase method ○ Study Conduct ▪ The study was conducted in the three clinical centres ▪ Patients were randomized to use three of the five SMBGs – stratified by centre ▪ SMBG measurements were done by the patients themselves. ▪ Patients were fasting. ▪ The reference test was done with capillary blood form the fingertips before and after the self-test (within 60 minutes of the self-test).	○ Difference between the SMBG evaluation and the reference test, measured using ▪ Mean bias ▪ MARD ▪ Pearson correlation coefficient ○ Differences between the difference SMBGs in terms of mean absolute bias ○ Compliance with ISO 15197:2003 accuracy requirements ○ Compliance with ISO 15197:2010 accuracy requirements ○ Performance of the SMBGs on error grids ▪ Clarke Grid ▪ Parkers Grid
Zueger et al. 2012[49] – Switzerland			
To evaluate and compare the reliability of three SMBGs. Diagnostic Study The source of funding wan not explicitly declared. However, it was reported that manufacturers of the evaluated devices did not financially supported the evaluation.	○ Trial size: 150 patients ○ Age ▪ mean (SD): 49.3 (1.3) years ○ Male patients (60.7%)	○ Intervention (Index test) ▪ Contour (Bayer) ▪ Accu-Check Aviva (Roche) ▪ FreeStyle Lite FreeStyle (Abbott) ○ Comparator (Reference test) ▪ HemoCue Glucose 201+ System (HemoCue AB) with plasma conversion ○ Study Conduct ▪ The study was conducted in an academic health facility ▪ SMBG measurements were done by healthcare provider ▪ Blood glucose was evaluated by the three SMBGs devices ▪ All measurements were done with capillary blood samples.	○ Difference between the SMBG evaluation and the reference test, measured by ▪ Mean bias (Bland-Altman method) ▪ MARD ○ Compliance with ISO 15197:2003 accuracy requirements ○ Performance of the SMBGs on error grids ▪ Clarke Grid

MARD= mean absolute relative difference – continuous measure that uses the magnitude of the relative difference for each observation; **SD=** standard deviation; **SMBG=** self-monitoring blood glucose device;

APPENDIX 6. Definition of The Accuracy Standards in the Included Studies

Accuracy standard	Description
ISO 151987[51]	Ninety-five percent (95%) of the individual glucose results shall fall within ± 0.83 mmol/liter (15 mg/dl)of the results of the manufacturer's measurement procedure at glucose concentrations ≤4.2 mmol/liter (75 mg/dl) and within ±20% at glucose concentrations >4.2 mmol/liter (75 mg/dl)
Parkes Error Grid[52]	Zone A are those values within 20% of the reference sensor, Zone B contains points that are outside of 20% but would not lead to inappropriate treatment, Zone C are those points leading to unnecessary treatment,
Clarke Error Grid[53]	Zone D are those points indicating a potentially dangerous failure to detect hypoglycemia or hyperglycemia, Zone E are those points that would confuse treatment of hypoglycemia for hyperglycemia and vice-versa.

APPENDIX 7. Critical Appraisal of the Included Studies

Strengths	Limitations
Tack et al. 2012[50] – Netherlands/ Germany	
○ The trial included patients with type I and type II diabetes; this type of patient represent the potential users of SMBGs ○ The trial used a standard reference test, the YSI 2300 glucose analyzer ○ Patients conducted the SMBG evaluation themselves; this will procedure provides strength to the trial because it imitates the real life practice ○ The reference test was done within 60 minutes of the index test; this would likely to minimize the effect of blood glucose variation	○ The trial evaluated five blood glucose monitoring devices, and each patient used three devices only. This would have impact on the comparisons between devices; however, because the distribution of SMBGs was randomized, this would minimize the potential of selective testing bias. ○ The statistical analysis excluded 48 patients who were enrolled and participated in the study. The publication did not report the device(s) which had been used by these excluded patients. The reasons for the exclusion were provided; however, this should be supplemented by the devices used to exclude the potential bias of selective testing. ○ The study did not report if the SMBG reading were conducted without knowing the reference test results ○ The reproducibility of the SMBG devices was not evaluated
Zueger et al. 2012[49] – Switzerland	
○ All devices in the study were tested by all included patients ○ All measurements, including the index test, were carried out with one single subsequent drop of blood from the same area. This would minimize the effect of blood glucose variation	○ The report did not specify the type of diabetes for the included patients. This may affect the generalizability of the study findings ○ The study used a reference test that is an SMBG. This device might not be an appropriate standard reference test. This would impact the comparison of the study findings with other studies that used different reference tests ○ The measurements were carried out by one healthcare provider. This was done to minimize the user dependant pre-analytical bias. However, this procedure may limit the generalizability of the findings since the SMBGs are usually used by the patients and not by their healthcare providers ○ The study did not report if the SMBG reading were conducted without knowing the reference test results ○ The reproducibility of the SMBG devices was not evaluated

APPENDIX 8. Summary of Study Findings

<table>
<tr><th colspan="7">Study Findings</th><th>Conclusions</th></tr>
<tr><td colspan="8">Tack et al. 2012[50] – Netherlands/ Germany</td></tr>
<tr><td colspan="7">○ Difference between the SMBG evaluation and the reference test:
<table>
<tr><th rowspan="2">Blood Glucose Meter</th><th rowspan="2">Subjects (n)/ Measurements (n)</th><th colspan="2">Mean bias</th><th rowspan="2">MARD (%)</th><th rowspan="2">Pearson correlation coefficient</th></tr>
<tr><th>mg/dl</th><th>%</th></tr>
<tr><td>FreeStyle Lite</td><td>240/ 480</td><td>0.8</td><td>1.0</td><td>4.9</td><td>0.985</td></tr>
<tr><td>FreeDom Lite</td><td>244/ 488</td><td>0.3</td><td>1.0</td><td>5.5</td><td>0.985</td></tr>
<tr><td>Accu-Check Aviva</td><td>252/ 504</td><td>7.2</td><td>5.3</td><td>6.8</td><td>0.989</td></tr>
<tr><td>Contour</td><td>255/ 510</td><td>-1.2</td><td>-0.2</td><td>9.0</td><td>0.966</td></tr>
<tr><td>OneTouch UltraEasy</td><td>246/ 492</td><td>6.3</td><td>4.6</td><td>9.7</td><td>0.974</td></tr>
</table>
MARD = mean absolute relative difference

○ Differences between the difference SMBGs in terms of mean absolute bias, % (P value)
<table>
<tr><th></th><th>FreeStyle Lite</th><th>FreeDom Lite</th><th>Accu-Check Aviva</th><th>Contour</th><th>OneTouch UltraEasy</th></tr>
<tr><td>FreeStyle Lite</td><td></td><td>-0.7 (0.2470)</td><td>-2.0 (0.0005*)</td><td>-4.2 (<0.0001*)</td><td>-4.8 (<0.0001*)</td></tr>
<tr><td>FreeDom Lite</td><td></td><td></td><td>-1.3 (0.0191)</td><td>-3.5 (<0.0001*)</td><td>-4.1 (<0.0001*)</td></tr>
<tr><td>Accu-Check Aviva</td><td></td><td></td><td></td><td>-2.2 (<0.0001*)</td><td>-2.8 (<0.0001*)</td></tr>
<tr><td>Contour</td><td></td><td></td><td></td><td></td><td>-0.6 (0.2658)</td></tr>
</table>
* statistically significant difference

○ Compliance with ISO 15197:2003 accuracy requirements
<table>
<tr><th>ISO 15197 version</th><th>FreeStyle Lite</th><th>FreeDom Lite</th><th>Accu-Check Aviva</th><th>Contour</th><th>OneTouch UltraEasy</th></tr>
<tr><td>2003</td><td>Yes</td><td>Yes</td><td>Yes</td><td>No</td><td>No</td></tr>
<tr><td>2010</td><td>Yes</td><td>Yes</td><td>No</td><td>No</td><td>No</td></tr>
</table>
○ Performance of the SMBGs on error grids, % in each zone
<table>
<tr><th></th><th>FreeStyle Lite</th><th>FreeDom Lite</th><th>Accu-Check Aviva</th><th>Contour</th><th>OneTouch UltraEasy</th></tr>
<tr><td>Clarke Grid</td><td>A= 98.8%,
B=1.3%</td><td>A=97.3%,
B=1.4%,
D=1.2%</td><td>A= 96.6%,
B=3.0%,
D=0.4%</td><td>A= 92.4%,
B=7.3%,
D=0.4%</td><td>A= 90.4%,
B=7.9%,
D=1.6%</td></tr>
<tr><td>Parkers Grid</td><td>A=99.4%,
B=0.6%</td><td>A=98.4%,
B=1.4%,
C=0.2%</td><td>98.8%,
B=1.2%,</td><td>A=95.3%,
B=4.7%</td><td>A=94.1%,
B=5.9%</td></tr>
</table></td><td>The study authors concluded that FreeDom Lite and FreeStyle Lite SMBGs were the most accurate and reliable blood glucose meters. However, this conclusion should be interpreted with caution because of the potential bias of selective testing. It should be noticed also that this study was funded by the Abbott Diabetes Care (the manufacturer of the above mentioned SMBGs).</td></tr>
</table>

<table>
<tr><th>Study Findings</th><th>Conclusions</th></tr>
<tr><td colspan="2">Zueger et al. 2012[49] – Switzerland</td></tr>
<tr><td>
○ Difference between the SMBG evaluation and the reference test:
<table>
<tr><th>Blood Glucose Meter</th><th>Subjects (n)</th><th>Mean bias, mg/dl</th><th>MARD (%)</th></tr>
<tr><td>Contour</td><td rowspan="3">150</td><td>-13.2</td><td>10.1</td></tr>
<tr><td>Accu-Check Aviva</td><td>-2.7</td><td>7.0</td></tr>
<tr><td>FreeStyle Lite</td><td>-6.3</td><td>7.8</td></tr>
</table>
MARD = mean absolute relative difference

○ Differences between the difference SMBGs in terms of mean absolute bias, P value
<table>
<tr><th>Blood Glucose Meter</th><th>Accu-Check Aviva</th><th>FreeStyle Lite</th></tr>
<tr><td>Contour</td><td><0.001*</td><td>0.001*</td></tr>
<tr><td>Accu-Check Aviva</td><td></td><td>0.67</td></tr>
</table>
* statistically significant

○ Performance of the SMBGs on error grids, % in each zone
<table>
<tr><th>Blood Glucose Meter</th><th>Clarke Grid</th></tr>
<tr><td>Contour</td><td>A= 94%, B=5.3%, D=0.7%</td></tr>
<tr><td>Accu-Check Aviva</td><td>A= 96%, B= 2.7%, D= 1.3%</td></tr>
<tr><td>FreeStyle Lite</td><td>A= 96%, B= 4.0%</td></tr>
</table>
</td><td>Study authors concluded that patients can rely on the results of the three devices. They also stated that Accu-Check and Free-Style tended to slightly outperform the Contour device.</td></tr>
</table>