CADTH Health Technology Review

Real-Time Continuous Glucose Monitoring: A Review of Guidelines

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Abbreviations

AACE	American Association of Clinical Endocrinology
ADA	American Diabetes Association
AGREE	Appraisal of Guidelines for Research and Evaluation
CGM	continuous glucose monitoring
isCGM	intermittently scanned continuous glucose monitoring
NICE	National Institute for Health and Care Excellence
rtCGM	real-time continuous glucose monitoring
RCT	randomized controlled trial
SMBG	self-monitoring of blood glucose

Key Messages

- Six evidence-based guidelines regarding the use of real-time continuous glucose monitoring in people living with type 1 or type 2 diabetes were included in this report. Three included guidelines were of high quality, while 3 guidelines were of moderate quality due to unclear reporting of methodological details.

- Four evidence-based guidelines strongly recommended the use of real-time continuous glucose monitoring in adults for the management of type 1 diabetes, based on intermediate- to high-quality evidence.

- Four guidelines recommended real-time continuous glucose monitoring for adults living with type 2 diabetes, based on low- to high-quality evidence.

- Three guidelines strongly recommended the use of real-time continuous glucose monitoring in children and young people living with type 1 diabetes, based on intermediate- to high-quality evidence.

- One guideline recommended real-time continuous glucose monitoring for children and young people with type 2 diabetes, based on expert consensus rather than evidence of clinical effectiveness.

Context and Policy Issues

Diabetes is a chronic condition in which the body is not able to produce enough insulin and/or properly use insulin.[1] The body needs insulin to use sugar as an energy source.[1] Type 1 diabetes is an autoimmune condition in which the insulin-producing beta cells of the pancreas are destroyed by the immune system.[1] Type 1 diabetes is often diagnosed in childhood and common presenting symptoms include frequent urination, excessive thirst, weight loss, and diabetic ketoacidosis (a potentially life-threatening complication of diabetes in which acids called ketones build up to dangerous levels in the body).[2,3] In addition, hypoglycemia-related changes can have a negative impact on the quality of life of people with type 1 diabetes and lead to hypoglycemia fears.[4] Type 2 diabetes is a condition that occurs when the body does not make enough insulin and/or does not respond to the insulin it makes.[1] In the early stages of type 2 diabetes, there may be no symptoms or only mild symptoms that can go unnoticed.[5] When symptoms are present, they can include frequent urination, excessive thirst and hunger, fatigue, blurry vision, slow-healing wounds, and tingling, pain, or numbness in the hands and/or feet.[5]

Approximately 3 million Canadians have diagnosed diabetes.[6] The most common type of diabetes in adults is type 2 diabetes, accounting for approximately 90% of adults living with diabetes in Canada.[7] In children and youth aged younger than 20 years in Canada, type 1 diabetes accounts for at least 85% of diabetes cases.[6]

All people living with type 1 diabetes and some people with type 2 diabetes need to take insulin to keep blood glucose levels within the target range.[1,8] There are many ways insulin therapy can be delivered, including multiple daily injections and insulin pumps.[8] Blood glucose monitoring is used in combination with insulin therapy to adjust insulin doses and maintain glucose control.[9] The traditional method for blood glucose monitoring is self-monitoring of blood glucose (SMBG) using a glucometer (also called capillary blood glucose monitoring).[10] SMBG requires a fingerstick to take a blood sample, which can be painful and

time-consuming.[11] Some people living with diabetes find it difficult to practice SMBG at the recommended rates (e.g., 6 to 10 times per day).[9] Additionally, nocturnal or asymptomatic hypoglycemia (low blood glucose) may not be recognized through SMBG.[11] Severe hypoglycemia can lead to coma or death.[11]

Continuous glucose monitoring (CGM) systems continuously measure the glucose concentration in the interstitial fluid and transfer the data to a receiver which displays the results.[11] These devices represent an alternative to SMBG for people living with diabetes. CGM systems typically consist of 3 components: a sensor inserted into the deepest layer of the skin, a transmitter attached to the sensor, and a receiver (monitor or smartphone) that displays the results.[11,12] There are 2 types of CGM systems available for personal use: real-time CGM (rtCGM) and intermittently scanned CGM (isCGM, also known as flash glucose monitoring).[11] rtCGM systems (e.g., Dexcom G6, Guardian Connect) measure the glucose values and automatically display a recent value.[11] rtCGM devices have the capability for alerts and alarms for current and/or impending glycemic events, such as hyperglycemia or hypoglycemia.[13] Some older rtCGM systems (e.g., Dexcom G5) require daily calibration with SMBG, whereas newer devices (e.g., Dexcom G6) do not.[13,14] The rtCGM sensor application site is typically the abdomen or gluteus area.[11,15]

Diabetes is regarded as a burdensome disease for health care systems because of the time and resource costs related to the management of diabetes and its complications.[6] The direct cost to the Canadian health care system for type 1 and type 2 diabetes was $3.8 million in 2020 and is estimated to climb to $4.9 million in 2030.[16] The financial burden of rtCGM use in patients is also high.[17] Many people in Canada with diabetes pay more than 3% of their income, or more than $1,500 per year, for prescribed medications, devices, and supplies; these out-of-pocket costs affect treatment adherence.[16]

In 2022, CADTH reviewed the clinical and cost-effectiveness of CGM in 3 rapid reviews: rtCGM compared to isCGM for people with diabetes,[18] rtCGM compared to SMBG for people with type 1 diabetes,[19] and rtCGM versus SMBG for people with type 2 diabetes.[20] The purpose of this rapid review is to summarize and critically appraise evidence-based guidelines regarding the use of rtCGM in people living with type 1 or type 2 diabetes.

Research Question

What are the evidence-based guidelines regarding the use of real-time continuous glucose monitoring in adult and pediatric populations living with type 1 or type 2 diabetes?

Methods

Literature Search Methods

A limited literature search was conducted by an information specialist on key resources including MEDLINE, Embase, the Cochrane Database of Systematic Reviews, the International HTA Database, and the websites of Canadian and major international health technology agencies, as well as a focused internet search. The search strategy comprised both controlled

vocabulary, such as the National Library of Medicine's MeSH (Medical Subject Headings), and keywords. The main search concepts were continuous glucose monitoring (CGM), real-time continuous glucose monitoring (rtCGM), type 1 diabetes, and type 2 diabetes. No filters were applied to limit the retrieval by study type. Comments, newspaper articles, editorials, letters, and conference abstracts were excluded.

Where possible, retrieval was limited to the human population. The search was completed on July 12, 2022, and limited to English-language documents published since January 1, 2017.

Selection Criteria and Methods

One reviewer screened citations and selected studies. In the first level of screening, titles and abstracts were reviewed and potentially relevant articles were retrieved and assessed for inclusion. The final selection of full-text articles was based on the inclusion criteria presented in Table 1.

Exclusion Criteria

Articles were excluded if they did not meet the selection criteria outlined in Table 1 or were published before 2020. Guidelines for pregnant people living with type 1 or type 2 diabetes were excluded. Guidelines with unclear methodology were also excluded.

Critical Appraisal of Individual Studies

The included publications were critically appraised by 1 reviewer using the Appraisal of Guidelines for Research and Evaluation (AGREE) II instrument[21] for guidelines. Summary scores were not calculated for the included studies; rather, the strengths and limitations of each included publication were described narratively.

Summary of Evidence

Quantity of Research Available

A total of 879 citations were identified in the literature search. Following screening of titles and abstracts, 874 citations were excluded and 5 potentially relevant reports from the

Table 1: Selection Criteria

Criteria	Description
Population	People living with type 1 or type 2 diabetes
Intervention	Real-time continuous glucose monitoring
Comparator	Not applicable
Outcomes	Recommendations regarding the appropriate use of real-time continuous glucose monitoring for adults and pediatric populations living with type 1 or type 2 diabetes (e.g., considerations for the implementation and use of real-time continuous glucose monitoring for adults and pediatric populations respectively)
Study designs	Evidence-based guidelines

electronic search were retrieved for full-text review. Six potentially relevant publications were retrieved from the grey literature search for full-text review. Of these 11 potentially relevant articles, 5 publications were excluded for various reasons, and 6 evidence-based guidelines met the inclusion criteria and were included in this report. Appendix 1 presents the PRISMA[22] flow chart of the study selection.

Additional references of potential interest are provided in Appendix 5.

Summary of Study Characteristics

Six evidence-based guidelines[10,23-27] were included in this report.

Five guidelines[10,23-25,27] reported their methodology in separate publications.[28-31] These documents were used to supplement the information summarized in this report.

Study Design

The American Diabetes Association (ADA) Standards of Medical Care for Diabetes[23] were updated in 2022. An extensive literature search was performed, and relevant literature was reviewed through July 1, 2021, with critical updates through August 1, 2021 considered. Recommendations were revised based on new evidence, new considerations for standard of care practices, or to clarify prior recommendations or revise wording to match the strength of the published evidence. Recommendations were assigned letter ratings depending on the quality of the evidence: A for well-conducted randomized controlled trials (RCTs) that are adequately powered or have compelling non-experimental evidence; B for well-conducted cohort studies or case-control studies; C for poorly controlled or uncontrolled studies or conflicting evidence with the weight of evidence supporting the recommendation; or E for expert census or clinical experience. The ADA Standards of Care[23] were reviewed by ADA's clinical staff leadership, and underwent annual review and approval by the board of directors.

The 3 National Institute for Health and Care Excellence (NICE) guidelines[10,24,25] were updated in 2022 and informed by systematic reviews of clinical effectiveness and cost-effectiveness. Systematic searches until May 2021 for relevant RCTs, systematic reviews of RCTs, and economic evaluations were undertaken. The NICE guidelines[10,24,25] used the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach to evaluate the quality of the evidence. The quality of evidence was graded from very low to high, and reflected the strength of recommendations in the wording (i.e., "offer/advise" was used for strong recommendations with clear evidence of benefit, while "consider" was used if the evidence was less certain). The committee discussed the evidence and drafted the recommendations. The committee moved from the evidence to each recommendation and discussed any issues that influenced their decision-making. In line with the GRADE principles on "evidence to decisions", summaries of the discussions described the relative value placed on outcomes, benefits and harms, resource use, and the overall quality of the evidence.[10,24,25]

The American Association of Clinical Endocrinology (AACE) guideline[26] was published in 2021 and informed by systematic searches between January 2012 and February 2021 for systematic reviews, RCTs, and non-randomized studies. Levels of evidence were assigned to included studies according to established AACE evidence ratings: strong (RCT or meta-analysis of only RCTs), intermediate (meta-analysis of non-randomized studies, network meta-analysis, non-randomized studies, epidemiological studies), or weak (discovery science, economic studies, case series, case reports, preclinical studies, basic science).[26] These ratings informed the confidence and strength of evidence in aggregate for each

recommendation: grades A (very strong), B (strong), C (not strong), and D (primarily based on expert opinion). Clinical questions provided the framework for the guidelines with answers in the form of recommendations. Final recommendations were based on discussion and unanimous consensus.[26]

The 2021 Diabetes Canada guideline on glucose monitoring in adults and children with diabetes[27] was an update to the 2018 recommendations for monitoring glycemic control. This 2021 report was developed based on a systematic search of the literature published from November 2017 to October 2020 to retrieve relevant articles published since the last literature search of the original report. The full-text citations and critical appraisal reports were prepared by the McMaster Evidence Review and Synthesis Team and reviewed by the expert working group, who graded the evidence and drafted the revised recommendations. Evidence levels were designated as follows: 1A for evidence obtained from a systematic review or meta-analysis of high-quality RCTs or an appropriately designed RCT with adequate power to answer the research question; 1B for a non-randomized clinical trial or cohort study with indisputable results; 2 for an RCT or systematic review that does not meet level 1 criteria; 3 for a non-randomized clinical trial or cohort study or systematic review or meta-analysis of non-randomized trials or cohort studies; and 4 for other studies. Grading of recommendations was based on the level of the best evidence: A (the best evidence was at level 1); B (level 2); C (level 3); and D (required best evidence at level 4 or consensus). The steering committee reviewed the cited evidence independently and suggested revisions to the draft recommendations and the text.[27] Final recommendations were unanimously approved by the steering committee.[27]

Country of Origin

The ADA guideline[23] and AACE guideline[26] were designed for use in the US. The 3 NICE guidelines[10,24,25] were intended to be applied in England. The Diabetes Canada guideline[27] was developed for Canada.

Patient Population

The target populations of 3 guidelines[23,26,27] were adults and children living with diabetes. The other 3 guidelines targeted adults with type 1 diabetes,[10] adults with type 2 diabetes,[25] and children and young people with type 1 diabetes.[10]

The intended users of 5 guidelines[10,23,24-26] were health care professionals and other key stakeholders. For the NICE guidelines,[10,24,25] the intended users also included people living with type 1 or type 2 diabetes, and their families and carers. The intended users of the Diabetes Canada guideline[27] were not explicitly reported, but can be deduced to be people living with diabetes and their health care providers.[27]

Interventions and Comparators

Recommendations that specified rtCCM in the 6 guidelines[10,23-27] were included. Five guidelines[10,23-26] made recommendations regarding any CGM systems, which include rtCGM and isCGM. Due to the large number and nature of these recommendations (e.g., general usage, patient education, discussing patient concerns),[10,23-26] only specific recommendations regarding the use of rtCGM were considered relevant for this report.

In the evidence synthesis for all guidelines,[10,23-27] the comparator was SMBG.

rtCGM was also compared to isCGM in the evidence synthesis for all guidelines.[10,23-27] isCGM systems (e.g., FreeStyle Libre) measure glucose levels every minute and store 1 value every 15 minutes. isCGM systems need to be actively scanned to display glucose information.[11] Only the most recent 8 hours of data are retained in isCGM systems and, therefore, the person using the system must scan the sensor at least every 8 hours to avoid data gaps.[13]

Outcomes

The primary outcomes in the 3 NICE guidelines[10,24,25] were hemoglobin A1C, time spent in target glucose range estimates, hypoglycemia, glycemic variability, mortality, and diabetic ketoacidosis. Secondary outcomes were other adverse events, mental health outcomes, awareness of hypoglycemia, adherence, and quality of life.[10,24,25] The 3 NICE guidelines[10,24,25] also considered cost-effectiveness.

Three guidelines[23,26,27] did not report on the outcomes considered during development, or if and which outcomes were eligible during selection of supporting evidence; however, evidence on hemoglobin A1C,[23,26,27] time in range estimates,[26,27] hypoglycemia,[23,26,27] quality of life,[23,26,27] and adverse events (e.g., severe hypoglycemia,[26,27] hospitalizations,[23] emergency department visits[23]) were mentioned in the recommendations and/or supporting evidence.[23,26,27]

Additional details regarding the characteristics of included publications are provided in Appendix 2.

Summary of Critical Appraisal

An overview of the critical appraisal of the included guidelines is summarized in the following text. Additional details regarding the strengths and limitations of the included guidelines are provided in Appendix 3.

With respect to scope and purpose, all guidelines[10,23-27] provided a clear description of their objectives and specified the target populations. The clinical research questions covered by the guidelines were reported in 4 guidelines,[10,24-26] but not in the ADA[23] and Diabetes Canada[27] guidelines.

The guideline development groups were comprised of clinical and methodological experts from multidisciplinary areas for all guidelines.[10,23-27] The NICE guidelines[10,24,25] included at least 2 lay members (patients with type 1 or type 2 diabetes and caregivers) on their guideline committees, and sought involvement from people with type 1 or 2 diabetes who use health and care services, family members, caregivers, and the public. For 3 guidelines,[23,26,27] the views and preferences of the target population were not sought and there was no mention of patient, parent, or caregiver representation or consultation.[23,26,27]

With respect to rigour of guideline development, systematic methods were used to search for evidence in all guidelines.[10,23-27] The NICE guidelines[10,24,25] provided full details of the strategy used to search for evidence. The ADA and Diabetes Canada guidelines[23,27] provided very brief details of their methodology; specifically, the undertaking of a literature review and the search time frame. However, it was not specified how the literature review process was carried out (e.g., databases searched, main search terms, inclusion criteria, how relevant studies were selected) in these 2 guidelines.[23,27] The authors of the AACE guideline[26] conducted literature searches in 1 database (i.e., PubMed), which may have resulted in omission of relevant information.

The link between the individual recommendations and supporting evidence was not completely evident in 5 guidelines.[10,23-27] Rather, each report[10,23-27] provided a section on the overall evidence for CGM or rtCGM. Therefore, the reasoning used to reach the individual recommendations was not always clear. Four guidelines[10,24-26] were externally reviewed by experts before publication, but 2 guidelines did not report how the guideline was validated.[23,27]

All guidelines[10,23-27] provided specific, unambiguous, and easily identifiable recommendations. The potential resource implications of applying the recommendations were considered in 4 guidelines,[10,24-26] but not in the ADA[23] and Diabetes Canada[27] guidelines.

Four guidelines[10,24-26] described their procedure for updating their guidelines. While it was reported that the ADA guideline[23] underwent an annual review, the procedure for guideline updates was not explicitly described.

Regarding editorial independence, it was uncertain whether the views of the funding body influenced the content of the included guidelines.[10,23-27] For each guideline,[10,23-27] the funding was provided by the professional organization (i.e., ADA, NICE, AACE, Diabetes Canada) that was responsible for creating the guidelines, and there was no explicit statement that the views of the funding body had not influenced the guideline. However, all guidelines[10,23-27] reported the competing interests of their authors.

In summary, the 3 NICE guidelines[10,24,25] followed a detailed process for developing the recommendations based on the criteria outlined in the AGREE II instrument.[21] The methodology of the AACE guideline[26,27] had some limitations. The ADA[23] and Diabetes Canada[27] guidelines did not report sufficient detail regarding the methodology used for developing their recommendations.

Additional details regarding the strengths and limitations of included publications are provided in Appendix 3.

Summary of Findings

Guidelines

Appendix 4 presents the main study findings and authors' conclusions.

Recommendations Regarding the Use of rtCGM for Adults With Type 1 Diabetes

The ADA Standards of Care[23] recommended rtCGM for adults with type 1 diabetes for diabetes management based on level A evidence (well-conducted and adequately powered RCTs; strength of recommendation not reported).

The NICE guideline for adults with type 1 diabetes[10] made a strong recommendation for the use rtCGM (level of evidence not reported). The NICE guideline[10] also strongly recommended the use of SMBG if a person could not or did not want to use rtCGM (level of evidence not reported).

The Diabetes Canada guideline[27] recommended rtCGM for adults with type 1 diabetes who were willing and able to use rtCGM devices on a near-daily basis (grade A recommendation, based on well-conducted RCTs). rtCGM was recommended versus SMBG (grade A recommendation, based on well-conducted RCTs) and isCGM (grade B recommendation, based on low- to moderate-quality RCTs).

The AACE guideline[26] strongly recommended rtCGM over isCGM for persons with diabetes (type not specified) with problematic hypoglycemia who required predictive alarms/alerts based on low- to intermediate-quality evidence. The AACE guideline[26] also very strongly recommended rtCGM for persons aged 65 years and older with insulin-requiring diabetes (type not specified), based on intermediate-quality evidence.

Recommendations Regarding the Use of rtCGM for Adults With Type 2 Diabetes

The ADA Standards of Care[23] recommended rtCGM for adults with type 2 diabetes for diabetes management, based on level A evidence (strength of recommendation not reported).

The NICE guideline for adults with type 2 diabetes[25] recommended rtCGM as an alternative to isCGM if available for the same or lower cost, based on evidence indicating that the benefit was less than certain.

The Diabetes Canada guideline[27] recommended rtCGM for adults with type 2 diabetes using basal-bolus therapy who had not achieved their hemoglobin A1C target and were willing and able to use rtCGM devices (grade A recommendation, based on well-conducted RCTs).

The AACE guideline[26] strongly recommended rtCGM over isCGM for persons with diabetes (type not specified) with problematic hypoglycemia who required predictive alarms/alerts based on low- to intermediate-quality evidence. The AACE guideline[26] also very strongly recommended rtCGM for persons 65 years of age and older with insulin-requiring diabetes (type not specified) based on intermediate-quality evidence.

Recommendations Regarding the Use of rtCGM for Children and Adolescents With Type 1 Diabetes

The ADA Standards of Care[23] recommended rtCGM for youth with type 1 diabetes for diabetes management, based on level B evidence (well-conducted cohort studies).

The NICE guideline for children and young people with type 1 diabetes[24] made a strong recommendation for the use of rtCGM (level of evidence not reported). The NICE guideline also made a strong recommendation for offering children and young people with type 1 diabetes a choice of rtCGM device, with a list of factors to consider when choosing a device (e.g., device accuracy, access to specific technologies, fear of hypoglycemia, device calibration, predictability of child or young person's activity, and blood glucose levels). The NICE guideline[24] also strongly recommended the use of isCGM for children and young people with type 1 diabetes who were unable to use rtCGM or expressed a clear preference for isCGM (level of evidence not reported). A strong recommendation was also made for the use capillary blood glucose monitoring for persons who could not or did not want to use rtCGM or isCGM (level of evidence not reported).[24]

The Diabetes Canada guideline[27] recommended rtCGM for children with type 1 diabetes who were willing and able to use rtCGM devices on a near daily basis (grade A recommendation, based on well-conducted RCTs).

Recommendations Regarding the Use of rtCGM for Children and Adolescents With Type 2 Diabetes

The ADA Standards of Care[23] recommended rtCGM for youth with type 2 diabetes for diabetes management, based on expert consensus or clinical expertise (in the absence of evidence from clinical studies).

Other Recommendations

The ADA Standards of Care[23] recommended that rtCGM be used as close to daily as possible for maximum benefit, based on level A evidence. The ADA guideline[23] also recommended periodic use of rtCGM or isCGM in circumstances where continuous use was not appropriate, desired, or available. The level of evidence supporting this recommendation was reported as C (poorly controlled or uncontrolled studies, or conflicting evidence), but the evidence itself was not reported.[23]

Limitations

Four guidelines[10,23,25,27] recommended rtCGM for people who had the ability to use rtCGM devices. For examples, the ADA Standards of Care[23] made recommendations for adults and youth "who are capable of using devices safely (either by themselves or with a caregiver)" and the NICE guidelines for adults with type 1[10] and type 2 diabetes[25] made recommendations for alternatives to rtCGM for people who "cannot use" rtCGM.[10] However, there was no further information or guidance provided in the guideline documents regarding how the clinician should determine if patients meet these requirements.[10,23,25]

CGM technologies are changing very quickly with increasing overlap between rtCGM and isCGM, as features such as predictive alerts or alarms (available in rtCGM devices) are added to newer isCGM devices.[10] The guideline authors acknowledged this, and therefore did not make recommendations on using specific devices, as such recommendations would soon be out of date.[10,23,24]

The Diabetes Canada guideline[23] was developed for the Canadian context, but was assessed as having a number of limitations due to incomplete reporting of the methods. The other 5 guidelines[10,23-26] were developed for use in the US[23,26] or England[10,24,25]; therefore, the generalizability of the recommendations to the Canadian context was unclear.

Conclusions and Implications for Decision- or Policy-Making

This report comprised 6 evidence-based guidelines[10,23-27] regarding the use of rtCGM in people living with type 1 or type 2 diabetes.

Of the included guidelines, 4[10,23,26,27] recommended the use of rtCGM by adults, including seniors (who are at significantly higher risk for severe hypoglycemia compared to younger people),[23,26] for the management of type 1 diabetes. This recommendation is aligned with the findings of the 2022 CADTH report on the clinical effectiveness and cost-effectiveness of rtCGM in type 1 diabetes.[19] The report concluded that rtCGM may have been favoured over SMBG in improving hemoglobin A1C, time in range outcomes, and severe hypoglycemia in adults with type 1 diabetes. The CADTH report[19] also found that rtCGM may be more cost-effective in the long term compared to SMBG in adults with type 1 diabetes.[19]

Four guidelines[23,25-27] recommended the use of rtCGM by adults with type 2 diabetes. This recommendation reflects the results of the 2022 CADTH report on the effectiveness of type 2 diabetes that rtCGM[20] may provide positive effects on hemoglobin A1C, with low rates of severe adverse events. However, the CADTH report found that rtCGM was not cost-effective compared to SMBG in people with type 2 diabetes.[20]

Three guidelines[23,24,27] recommended the use of rtCGM for children and young people with type 1 diabetes. This also reflects the findings of the 2022 CADTH report on the effectiveness of type 1 diabetes[19] that rtCGM may provide positive effects on hemoglobin A1C, time in range, time above range, and treatment satisfaction in children and pediatric patients with type 1 diabetes.

Overall, the strength of these recommendations ranged from less than certain to very strong and were based on evidence that ranged in quality from very low to high.[10,23,26,27] The quality of the clinical and cost-effectiveness evidence of rtCGM (as assessed by systematic review authors) was also found to range from very low to high-quality in the 2 CADTH reports on type 1 and type 2 diabetes.[19,20] Recommendations emphasized patient choice and suggested that adherence to rtCGM was likely to be higher if the device was matched to a person's needs and preferences.[10,23-25,27]

The authors of the Diabetes Canada guideline[27] and the NICE guideline for children and young people[24] acknowledged that there was a lack of evidence on the clinical effectiveness of rtCGM in children and young people with type 2 diabetes. The CADTH report on the clinical and cost-effectiveness of rtCGM in type 2 diabetes[20] also reported no evidence in pediatric patients. Diabetes Canada[27] and NICE[24] did not make recommendations for the use of rtCGM for children and young people with type 2 diabetes. Rather the NICE guideline[24] made a recommendation for research on continuous glucose monitoring in children and young people living with type 2 diabetes. On the other hand, the ADA guideline[23] recommended rtCGM for youth with type 2 diabetes based on expert consensus and/or clinical expertise, in the absence of evidence of clinical effectiveness.

Five guidelines[23,24,25,26,27] recommended rtCGM more favourably than isCGM for diabetes management. The NICE guideline for adults with type 1 diabetes[10] recommended both rtCGM and isCGM, due to the very low certainty of the evidence on comparative clinical effectiveness between the 2 CGM technologies.

In general, there was agreement across guidelines on the use of rtCGM for the management of type 1 and 2 diabetes in adults and pediatric populations. However, the variation in the strengths of recommendations and heterogeneity in the quality of evidence should be considered when interpreting the findings of this report. Guidelines developed with rigorous methodology that are specific to the Canadian context would provide additional guidance in use of rtCGM for diabetes management in a more local context.
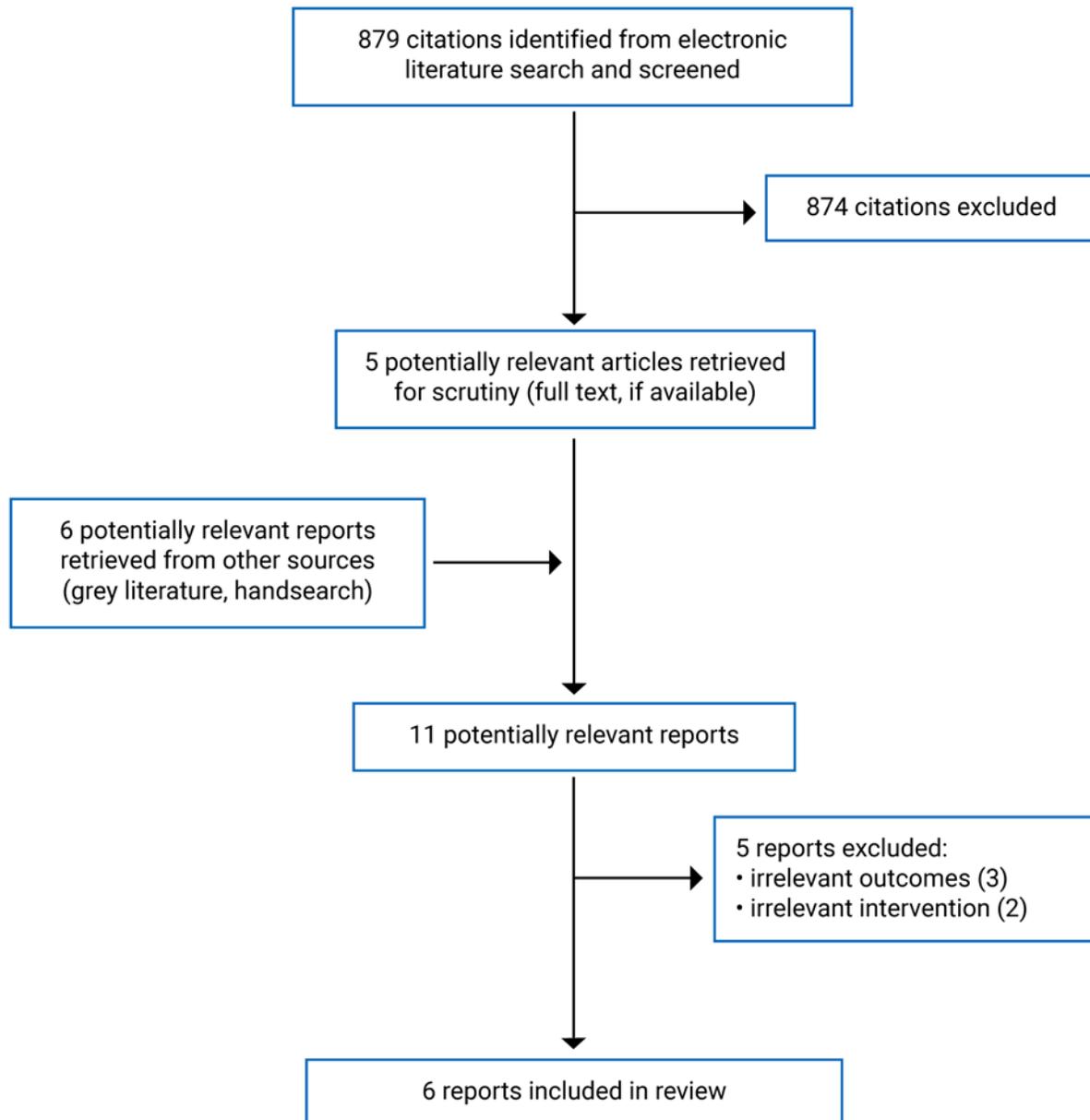
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Appendix 1: Selection of Included Studies

Figure 1: Selection of Included Studies

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┌──────────────────────────────────────┐
│  879 citations identified from        │
│  electronic literature search         │
│  and screened                         │
└──────────────────────────────────────┘
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                 │──────────────────► ┌──────────────────────────┐
                 │                    │  874 citations excluded  │
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┌──────────────────────────────────────┐
│  5 potentially relevant articles      │
│  retrieved for scrutiny               │
│  (full text, if available)            │
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┌──────────────────────────────┐       │
│  6 potentially relevant       │──────►│
│  reports retrieved from       │       │
│  other sources (grey          │       ▼
│  literature, handsearch)      │   ┌──────────────────────────────┐
└──────────────────────────────┘   │  11 potentially relevant      │
                                    │  reports                      │
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                 │                    │  5 reports excluded:         │
                 │                    │  • irrelevant outcomes (3)   │
                 ▼                    │  • irrelevant intervention (2)│
┌──────────────────────────────────────┐ └──────────────────────────────┘
│  6 reports included in review         │
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Appendix 2: Characteristics of Included Publications

Table 2: Characteristics of Included Guidelines

Intended users, target population	Intervention and practice considered	Major outcomes considered	Evidence collection, selection, and synthesis	Evidence quality assessment	Recommendations development and evaluation	Guideline validation
ADA guideline, 2022[23,29,30]						
Intended users: Clinicians, researchers, policy-makers, and other interested individuals with components of diabetes care, general treatment goals, and tools to evaluate quality of care **Target population**: Patients with diabetes, including children from birth to 11 years of age and adolescents aged 12 to 18 years, and older adults (aged 65 years and older)	Diabetes technology for patients with diabetes **Relevant intervention**: rtCGM	• Hemoglobin A1C • Adverse events (hypoglycemia episodes, ED visits, hospitalization) • QoL	Evidence collected using a systematic literature review, with critical updates	Ratings depended on quality of evidence in support of the recommendation: • A = Clear evidence from well-conducted, generalizable RCTs that are adequately powered (e.g., well-conducted multi-centre RCT, MA incorporating quality ratings in the analysis; or compelling non-experimental evidence ("all or none" rule developed by University of Oxford CEBM); or supportive evidence from well-conducted, adequately powered RCTs (e.g., well-conducted RCT at 1 or more institutions, MA with quality ratings) • B = Supportive evidence from well--	Existing recommendations were updated based on new evidence, new considerations for standard of care practices, or, in some cases, to clarify the prior recommendations or revise wording to match the strength of the published evidence. The literature review is supplemented with input from ADA staff and the medical community at large. Annual review and approval by the ADA board of directors, which includes health care professionals, scientists, and lay people. Review by the ADA scientific and medical staff.	Feedback by the larger clinical community was welcome, and readers were invited to comment online.

Intended users, target population	Intervention and practice considered	Major outcomes considered	Evidence collection, selection, and synthesis	Evidence quality assessment	Recommendations development and evaluation	Guideline validation
				conducted cohort studies (e.g., well-conducted prospective cohort study or registry, MA or well-conducted cohort studies) or well-conducted case-control study • C = Supportive evidence from poorly controlled (e.g., RCTs with 1 or more major or 3 minor methodological flaws) or uncontrolled studies (e.g., observational studies with high potential for bias; case series or case reports) or conflicting evidence with the weight of evidence supporting the recommendation • E = Expert census or clinical experience in the case of no evidence from clinical trials, clinical trials may be impractical, or there is conflicting evidence		

Intended users, target population	Intervention and practice considered	Major outcomes considered	Evidence collection, selection, and synthesis	Evidence quality assessment	Recommendations development and evaluation	Guideline validation
NICE NG 17 guideline, 2022[24,28]						
Intended users: Health care professionals, including those working in dental services; commissioners and providers; children and young people with T1D and T2D, and their families and carers **Target population**: Children and young people (aged < 18 years) with T1D and T2D	Diagnosis and management of T1D and T2D in children and young people **Relevant intervention**: rtCGM	• Hemoglobin A1C • Glucose TIR metrics • Glycemic variability • Mortality • Adverse events (hypoglycemia, DKA, hospitalization, SAEs) • Mental health outcomes • QoL • Cost-effectiveness	Evidence collected using a systematic evidence review of clinical and cost-effectiveness	Evidence quality was assessed using the GRADE approach. Strength of recommendation was reflected in the wording: • "Offer'" (or words such as "measure", "advise", or "refer") was used to reflect a strong recommendation, usually where there is clear evidence of benefit. • "Consider" was used to reflect a recommendation for which the evidence of benefit is less certain.	The committee discussed the evidence and drafted the recommendations. The committee moved from the evidence to each recommendation discussed any issues influenced their decision-making. In line with the GRADE principles on "evidence to decisions", summaries of the discussions described the relative value placed on outcomes, benefits and harms, resource use, and the overall quality of the evidence, as well as other considerations.	Registered stakeholders comment on the draft scope and draft guideline. NICE formally responds to comments from stakeholders, and these responses are published on the NICE website. Regular consultation allows organizations and individuals to comment on the recommendations. Once published, the guidelines are regularly checked, and updated in light of new evidence or intelligence, if necessary.
NICE N18 guideline, 2022[10,28]						
Intended users: Health care professionals, including those working in	Diagnosis and management of T1D in adults **Relevant**	• Hemoglobin A1C • Glucose TIR metrics • Glycemic variability	Evidence collected using a systematic evidence review of clinical and cost-effectiveness	Evidence quality was assessed using the GRADE approach. Strength of recommendation was	The committee discussed the evidence and drafted the recommendations. The committee moved from the evidence to	Registered stakeholders comment on the draft scope and draft guideline.

Intended users, target population	Intervention and practice considered	Major outcomes considered	Evidence collection, selection, and synthesis	Evidence quality assessment	Recommendations development and evaluation	Guideline validation
dental services; commissioners and providers; adults with T1D, and their families and carers **Target population**: Adults with T1D (aged ≥ 18 years)	**intervention**: rtCGM	• Mortality • Adverse events (hypoglycemia, DKA, hospitalization, SAEs) • Mental health outcomes • QoL • Cost-effectiveness		reflected in the wording: • "Offer" (or words such as "measure", "advise", or "refer") was used to reflect a strong recommendation, usually where there is clear evidence of benefit. • "Consider" was used to reflect a recommendation for which the evidence of benefit is less certain.	each recommendation discussed any issues influenced their decision-making. In line with the GRADE principles on "evidence to decisions", summaries of the discussions described the relative value placed on outcomes, benefits and harms, resource use, and the overall quality of the evidence, as well as other considerations.	NICE formally responds to comments from stakeholders, and these responses are published on the NICE website. Regular consultation allows organizations and individuals to comment on the recommendations. Once published, the guidelines are regularly checked, and updated in light of new evidence or intelligence, if necessary.
NICE N28 guideline, 2022[25,28]						
Intended users: Health care professionals, including those working in dental services; commissioners and providers; adults with T2D, and their families and carers **Target population**:	Management of T2D in adults **Relevant intervention**: rtCGM	• Hemoglobin A1C • Glucose TIR metrics • Glycemic variability • Mortality • Adverse events (hypoglycemia, DKA, hospitalization, SAEs)	Evidence collected using a systematic evidence review of clinical and cost-effectiveness	Evidence quality was assessed using the GRADE approach. Strength of recommendation was reflected in the wording: • "Offer" (or words such as "measure", "advise", or "refer") was used to reflect a strong recommendation,	The committee discussed the evidence and drafted the recommendations. The committee moved from the evidence to each recommendation discussed any issues influenced their decision-making. In line with the GRADE principles on "evidence to decisions", summaries of the	Registered stakeholders comment on the draft scope and draft guideline. NICE formally responds to comments from stakeholders, and these responses are published on the NICE website.

Intended users, target population	Intervention and practice considered	Major outcomes considered	Evidence collection, selection, and synthesis	Evidence quality assessment	Recommendations development and evaluation	Guideline validation
Adults with T2D (aged ≥ 18 years)		• Mental health outcomes • QoL • Cost-effectiveness		usually where there is clear evidence of benefit. • "Consider" was used to reflect a recommendation for which the evidence of benefit is less certain.	discussions described the relative value placed on outcomes, benefits and harms, resource use, and the overall quality of the evidence, as well as other considerations.	Regular consultation allows organizations and individuals to comment on the recommendations. Once published, the guidelines are regularly checked, and updated in light of new evidence or intelligence, if necessary.
AACE guideline, 2021[26]						
Intended users: Clinicians, diabetes care teams, health care professionals, other stakeholders **Target population**: People with diabetes	Use of advanced technology in the management of person with diabetes mellitus **Relevant intervention**: rtCGM	• Hemoglobin A1C • Glucose TIR metrics • Adverse events (hypoglycemia)	Evidence collected through comprehensive literature reviews	Grades for strength of recommendation: • A = very strong • B = strong • C = not strong • D = primarily based on expert opinion Levels of evidence: • Strong = RCT or MA of only RCTs • Intermediate = MA or non-randomized prospective or case-controlled trials, NMA, NRS (or unconfirmed randomization), prospective cohort	To develop the recommendations, the task force discussed the evidence found in the literature. When the task force determined guidance to be necessary despite a lack of available supporting literature, a recommendation was developed based on expert opinion and consensus of task force authors' collective experience, knowledge, and judgment. The recommendation grades and grades for strength of evidence	Drafts of the guidelines were reviewed and approved by all task force members, external reviewers, oversight committee, AACE board of directors, and peer reviewers for the journal *Endocrine Practice*.

Intended users, target population	Intervention and practice considered	Major outcomes considered	Evidence collection, selection, and synthesis	Evidence quality assessment	Recommendations development and evaluation	Guideline validation
				study, retrospective case-control study, nested case-control study, cross-sectional study, epidemiological study (hypothesis driven, survey, registry, data-mining) open-label extension study, or post-hoc analysis study • Weak = discovery science (explorative/ inductive, big data, network analysis, systems biology, Bayesian inference, modelling), economic study (Markov models, pharmacoeconomics), consecutive case series, single case report, preclinical study (feasibility, safety), basic research (must be high impact and relevant) • No conclusive evidence and/or expert opinion = no evidence (theory, opinion, consensus, review, position, policy, guideline) or other (lower impact/relevant	were confirmed through discussion and consensus. The final guideline document was also discussed to achieve unanimous consensus for each recommendation.	

Intended users, target population	Intervention and practice considered	Major outcomes considered	Evidence collection, selection, and synthesis	Evidence quality assessment	Recommendations development and evaluation	Guideline validation
				basic research, any flawed study)		
Diabetes Canada, 2021[27,31]						
Intended users: Clinicians, health care professions **Target population**: Adults, children, adolescents, and pregnant women with diabetes	Blood glucose monitoring in adults and children with diabetes **Relevant intervention**: rtCGM	• Hemoglobin A1C • TIR metrics • Adverse events (hypoglycemia events, severe hypoglycemia) • QoL	Evidence collected through systematic literature reviews	Criteria for assigning levels of evidence to published studies: • Level 1 = SR or MA or high-quality RCTs, or appropriately designed RCT with adequate power to answer the question posed by the investigators • Level 1B = non-randomized clinical trial or cohort study with indisputable results • Level 2 = RCT or SR that does not meet Level 1 criteria • Level 3 = non-randomized clinical trial or cohort study; SR or MA of non-randomized studies • Level 4 = other Criteria for assigning grades of recommendations for clinical practice:	The expert working group reviewed the citations, graded the evidence, drafted the revised recommendations, and created the initial draft of the preamble document to accompany the revised recommendations. The steering committee reviewed the cited evidence independently and suggested revisions to the draft recommendations and the text. The grading of the recommendations ware reviewed independently by the Independent Methods Review co-chair. The finalized recommendations were unanimously approved by the steering committee.	NR

Intended users, target population	Intervention and practice considered	Major outcomes considered	Evidence collection, selection, and synthesis	Evidence quality assessment	Recommendations development and evaluation	Guideline validation
				• A = best evidence at Level 1 • B = best evidence at Level 2 • C = best evidence at Level 3 • D = best evidence at Level 4 or consensus		

AACE = American Association of Clinical Endocrinology; ADA = American Diabetes Association; AGREE II = Appraisal of Guidelines for Research and Evaluation II; CEBM = Centre for Evidence-Based Medicine; DKA = diabetic ketoacidosis; ED = emergency department; GRADE = Grading of Recommendations, Assessment, Development, and Evaluation; MA = meta-analysis; NICE = National Institute for Health and Care Excellence; NMA = network meta-analysis; NRS = non-randomized study; QoL = quality of life; RCT = randomized controlled trial; rtCGM = real-time continuous glucose monitoring; SAE = severe adverse events; SMBG = self-monitoring of blood glucose; T1D = type 1 diabetes; T2D = type 2 diabetes; TIR = time in range.

Note that this table has not been copy-edited.

Appendix 3: Critical Appraisal of Included Publications

Note that this appendix has not been copy-edited.

Table 3: Strengths and Limitations of Guidelines Using AGREE II[21]

Item	ADA guideline, 2022[23]	NICE N17 guideline, 2022[10]	NICE NG 18 guideline, 2022[24]	NICE N28 guideline, 2022[25]	AACE guideline, 2021[26]	Diabetes Canada, 2021[27]
Domain 1: Scope and purpose						
1. The overall objective(s) of the guideline is (are) specifically described.	Yes	Yes	Yes	Yes	Yes	Yes
2. The health question(s) covered by the guideline is (are) specifically described.	No	Yes	Yes	Yes	Yes	No
3. The population (e.g., patients, public) to whom the guideline is meant to apply is specifically described.	Yes	Yes	Yes	Yes	Yes	Yes
Domain 2: Stakeholder involvement						
4. The guideline development group includes individuals from all relevant professional groups.	Yes	Yes	Yes	Yes	Yes	Yes
5. The views and preferences of the target population (e.g., patients, public) have been sought.	No	Yes	Yes	Yes	No	No
6. The target users of the guideline are clearly defined.	Yes	Yes	Yes	Yes	Yes	Partially
Domain 3: Rigour of development						
7. Systematic methods were used to search for evidence.	Yes	Yes	Yes	Yes	Yes	Yes
8. The criteria for selecting the evidence are clearly described.	No	Yes	Yes	Yes	Partially	Partially
9. The strengths and limitations of the body of evidence are clearly described.	Yes	Yes	Yes	Yes	Yes	Yes
10. The methods for formulating the recommendations are clearly described.	No	Yes	Yes	Yes	Yes	Yes
11. The health benefits, side effects, and risks have been considered in formulating the recommendations.	Yes	Yes	Yes	Yes	Yes	Yes

Item	ADA guideline, 2022[23]	NICE N17 guideline, 2022[10]	NICE NG 18 guideline, 2022[24]	NICE N28 guideline, 2022[25]	AACE guideline, 2021[26]	Diabetes Canada, 2021[27]
12. There is an explicit link between the recommendations and the supporting evidence.	Partially[1]	Partially[1]	Partially[1]	Partially[1]	Yes	Partially[1]
13. The guideline has been externally reviewed by experts prior to its publication.	No	Yes	Yes	Yes	Yes	No
14. A procedure for updating the guideline is provided.	No	Yes	Yes	Yes	Yes	No
Domain 4: Clarity of presentation						
15. The recommendations are specific and unambiguous.	Yes	Yes	Yes	Yes	Yes	Yes
16. The different options for management of the condition or health issue are clearly presented.	Yes	Yes	Yes	Yes	Yes	Yes
17. Key recommendations are easily identifiable.	Yes	Yes	Yes	Yes	Yes	Yes
Domain 5: Applicability						
18. The guideline describes facilitators and barriers to its application.	No	Yes	Yes	Yes	No	No
19. The guideline provides advice and/or tools on how the recommendations can be put into practice.	No	Partially	Partially	Partially	Yes	No
20. The potential resource implications of applying the recommendations have been considered.	No	Yes	Yes	Yes	Yes	No
21. The guideline presents monitoring and/or auditing criteria.	No	Yes	Yes	Yes	No	No
Domain 6: Editorial independence						
22. The views of the funding body have not influenced the content of the guideline.	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear
23. Competing interests of guideline development group members have been recorded and addressed.	Yes	Yes	Yes	Yes	Yes	Yes

AACE = American Association of Clinical Endocrinology; ADA = American Diabetes Association; AGREE II = Appraisal of Guidelines for Research and Evaluation II; NICE = National Institute for Health and Care Excellence.

[1]The supporting evidence is presented in a separate section on CGM or rtCGM, but not linked to the individual recommendations.

Appendix 4: Summary of Recommendations in Included Guidelines

Note that this appendix has not been copy-edited.

Table 4: Summary of Recommendations in Included Guidelines

Recommendations and supporting evidence	Strength of recommendations and level of evidence
ADA guideline, 2022[23]	
Recommendations for blood glucose monitoring in diabetes care **Recommendation 7.11:** "Real-time continuous glucose monitoring **A** or intermittently scanned continuous glucose monitoring **B** should be offered for diabetes management in adults with diabetes on multiple daily injections or continuous subcutaneous insulin infusion who are capable of using devices safely (either by themselves or with a caregiver). The choice of device should be made based on patient circumstances, desires, and needs." (p. S100) **Supporting evidence:** Multiple RCTs were performed using rtCGM devices, and the results were largely positive in terms of reducing hemoglobin A1C levels and/or episodes of hypoglycemia as long as participants regularly wore the devices. The initial RCTs were primarily done in adults with T1D on CSII and/or MDI. The primary outcome was met and showed benefit in adults of all ages including seniors. In adults with T1D, 3 RCTs compared isCGM and rtCGM. In 2 of the studies, the primary outcome was a reduction in time spent in hypoglycemia, and rtCGM showed benefit compared with isCGM. In the other study, the primary outcome was improved TIR, and rtCGM also showed benefit compared with isCGM. A retrospective analysis also showed improvement in TIR comparing rtCGM with isCGM. RCT data on rtCGM use in individuals with T2D on MDI and mixed therapies have consistently shown reductions in hemoglobin A1C but not a reduction in rates of hypoglycemia. The improvements in T2D largely occurred without changes in insulin doses or other diabetes medications. Retrospective data from rtCGM use in a Veterans Affairs population with TID and T2D treated with insulin show that use of rtCGM significantly lowered hemoglobin A1C and reduced rates of emergency department visits or hospitalizations for hypoglycemia, but did not significantly lower overall rates of emergency department visits, hospitalizations, or hyperglycemia.	**Strength of recommendation:** NR **Level of evidence:** A (clear evidence from well-conducted RCTs that are adequately powered)
Recommendation 7.12: "Real-time continuous glucose monitoring **A** or intermittently scanned continuous glucose monitoring **C** can be used for diabetes management in adults with diabetes on basal insulin who are capable of using devices safely (either by themselves or with a caregiver). The choice of device should be made based on patient circumstances, desires, and needs." (p. S100) **Supporting evidence:** Refer to evidence for Recommendation 7.11 RCT data on rtCGM use in individuals with T2D on basal insulin have consistently shown reductions in hemoglobin A1C but not a reduction in rates of hypoglycemia.	**Strength of recommendation:** NR **Level of evidence:** A

Recommendations and supporting evidence	Strength of recommendations and level of evidence
Recommendation 7.13: "Real-time continuous glucose monitoring **B** or intermittently scanned continuous glucose monitoring **E** should be offered for diabetes management in youth with type 1 diabetes on multiple daily injections or continuous subcutaneous insulin infusion who are capable of using the device safely (either by themselves or with a caregiver). The choice of device should be made based on patient circumstances, desires, and needs." (p. S100) **Supporting evidence:** In 3 RCTs in youth with T1D on CSII and/or MDI, data were less consistent than in adults with T1D.	**Strength of recommendation:** NR **Level of evidence:** B (supporting evidence from well-conducted cohort studies)
Recommendation 7.14: "Real-time continuous glucose monitoring or intermittently scanned continuous glucose monitoring should be offered for diabetes management in youth with type 2 diabetes on multiple daily injections or continuous subcutaneous insulin infusion who are capable of using devices safely (either by themselves or with a caregiver). The choice of device should be made based on patient circumstances, desires, and needs." (p. S100) **Supporting evidence:** NR	**Strength of recommendation:** NR **Level of evidence:** E (expert consensus or clinical experience)
Recommendation 7.15: "In patients on multiple daily injections and continuous subcutaneous insulin infusion, rt CGM devices should be used as close to daily as possible for maximal benefit. **A**" (p. S100) **Supporting evidence:** Multiple RCTs were performed using rtCGM devices, and the results were largely positive in terms of reducing hemoglobin A1C levels and/or episodes of hypoglycemia as long as participants regularly wore the devices.	**Strength of recommendation:** NR **Level of evidence:** A
Recommendation 7.17: "Periodic use of real-time or intermittently scanned continuous glucose monitoring or use of professional continuous glucose monitoring can be helpful for diabetes management in circumstances where continuous use of continuous glucose monitoring is not appropriate, desired, or available. **C**" (pages S100 to S101) **Supporting evidence:** NR	**Strength of recommendation:** NR **Level of evidence:** C (supportive evidence from poorly controlled or uncontrolled studies or conflicting evidence with the weight of evidence supporting the recommendation)
NICE N17 guideline, 2022[10]	
Recommendations for management of adults with T1D: CGM **Recommendation 1.6.10:** "Offer adults with type 1 diabetes a choice of real-time continuous glucose monitoring (rtCGM) or intermittently scanned continuous glucose monitoring (isCGM, commonly referred to as 'flash'), based on their individual preferences, needs, characteristics, and the functionality of the devices available." (p. 18) **Supporting evidence:** The committee agreed that there was enough evidence in key outcomes, such as hemoglobin A1C, time in range, and severe or nocturnal hypoglycemia, to demonstrate that rtCGM provided clinical benefits over standard SMG. However, they considered the evidence for rtCGM compared with isCGM was not good enough in terms of quality or sample size to clearly show clinical benefits of 1 technology over the other. The health economic modelling found that, when benefit of reduced fear of hypoglycemia with CGM was included, both rtCGM and isCGM	**Strength of recommendation:** Reflected in the wording: • Strong recommendations (clear evidence of benefit) contained the word "offer" (or words such as "measure", "advise", or "refer"). • Recommendations for which the evidence of benefit was less than certain contained the word "consider". **Level of evidence:** Reported in separate publication of evidence review for guideline, but not reported for each recommendation or in guideline document.

Recommendations and supporting evidence	Strength of recommendations and level of evidence
were cost-effective for the full population of adults with T1D compared with standard SMBG.	
Recommendation 1.6.14: "If a person cannot use or does not want rtCGM or isCGM, offer capillary blood glucose monitoring." (p. 20) **Supporting evidence**: NR	
NICE NG 18 guideline, 2022[24]	
Recommendations for management of T1D in children and young people: CGM **Recommendation 1.2.60:** "Offer real-time continuous glucose monitoring (rtCGM) to all children and young people with type 1 diabetes, alongside education to support children and young people and their families and carers to use it." (p. 15) **Supporting evidence:** The evidence on rtCGM showed it led to a decrease in hemoglobin A1C and an increase in time in range. This reflected the committee's experience in clinical practice. Because the evidence showed similar benefits of rtCGM for children and young people as for adults, the committee extrapolated the cost-effectiveness results from adults, concluding that rtCGM was cost-effective in this population.	**Strength of recommendation:** Reflected in the wording: - Strong recommendations (clear evidence of benefit) contained the word "offer" (or words such as "measure", "advise", or "refer"). - Recommendations for which the evidence of benefit was less than certain contained the word "consider". **Level of evidence:** Reported in separate publication of evidence review for guideline,[32] but not reported for each recommendation or in guideline document.
Recommendation 1.2.61: "Offer intermittently scanned continuous glucose monitoring (isCGM, commonly referred to as 'flash') to children and young people with type 1 diabetes aged 4 years and over who are unable to use rtCGM or who express a clear preference for isCGM." (pages 15 to 16) **Supporting evidence:** Since the same clinical benefits were not found for isCGM in children and young people as in adults, the committee agreed those cost-effectiveness findings could not be extrapolated, so they could not conclude that isCGM was a cost-effective technology for the full population of children and young people. They therefore agreed that isCGM should be restricted to children and young people who were unable or did not want to use rtCGM, or who preferred isCGM. Children and young people who preferred isCGM were likely to have better adherence with this type of device, so it would provide more benefit.	
Recommendation 1.2.62: "Offer children and young people with type 1 diabetes a choice of rtCGM device, based on their individual preferences, needs, characteristics, and the functionality of the devices available. See box 1 for examples of factors to consider as part of this discussion." (p. 16) **Supporting evidence**: NR	
Recommendation 1.2.66: "If a person cannot use or does not want rtCGM or isCGM, offer capillary blood glucose monitoring." (p. 18) **Supporting evidence**: NR	
NICE N28 guideline, 2022[25]	
Recommendations for management of adults with T2D: CGM **Recommendation 1.6.19:** "Consider real-time continuous glucose	**Strength of recommendation:** Reflected in the wording:

Recommendations and supporting evidence	Strength of recommendations and level of evidence
monitoring (rtCGM) as an alternative to isCGM for adults with insulin-treated type 2 diabetes if it is available for the same or lower cost." (p. 12) **Supporting evidence:** There was no evidence that rtCGM was cost-effective for people with T2D, so the committee agreed it could not be recommended for all adults with T2D (whether or not they used insulin). They noted, however, that prices of rtCGM had reduced over the past few years, and if this continued to happen there may come a time when it was no more expensive than isCGM. rtCGM would be an appropriate alternative for people who met the criteria for isCGM.	• Strong recommendations (clear evidence of benefit) contained the word "offer" (or words such as "measure", "advise", or "refer"). • Recommendations for which the evidence of benefit was less than certain contained the word "consider". **Level of evidence:** Reported in separate publication of evidence review for guideline, but not reported for each recommendation or in guideline document.
Recommendation 1.6.22: "If a person is offered rtCGM or isCGM but cannot or does not want to use any of these devices, offer capillary blood glucose monitoring." (p. 13) **Supporting evidence**: Although many people will choose CGM if offered, there are some people who either cannot be offered it or do not want to use it. Because it was still important for these people to monitor their blood glucose levels, the committee made a recommendation to reinforce the importance of offering capillary blood glucose monitoring instead.	
AACE Guideline, 2021[26]	
Recommendations for the use of advanced technology in the management of people with diabetes mellitus **When is one method of CGM (rtCGM vs isCGM) preferred over the other?** **Recommendation 2.3.1:** "rtCGM should be recommended over isCGM to persons with diabetes with problematic hypoglycemia (frequent/severe hypoglycemia, nocturnal hypoglycemia, hypoglycemia unawareness) who require predictive alarms/alerts; however, the lifestyle of persons with diabetes and other factors should also be considered." (pages 519 to 520) **Supporting evidence:** Studies comparing rtCGM and isCGM were sparse. Available evidence showed that rtCGM was superior to isCGM, when these systems did not include threshold alarms, in reducing hypoglycemia and improving TIR in adults with T1D with normal hypoglycemia awareness. Apart from hypoglycemia risk, reviews suggested that rtCGM may be preferred for persons with diabetes who were physically active or had busy lifestyles that would inhibit frequent scanning of an isCGM sensor, required uninterrupted monitoring by parents/caregivers, chose to use advanced insulin delivery technologies, or could not achieve desired glycemic targets with isCGM.	**Strength of recommendation:** Grade B (strong) **Level of evidence:** Low-intermediate strength of evidence
In what settings or special situations is use of diabetes technologies beneficial? **Recommendation 2.10.2:** "rtCGM is recommended for persons ≥65 years old with insulin-requiring diabetes to achieve improved glycemic control, reduce episodes of severe hypoglycemia, and improve QoL; however, glycemic goals should be individualized due to increased comorbidities and reduced capacity to detect and counter-regulate	**Strength of recommendation:** Grade A (very strong) **Level of evidence:** Intermediate strength of evidence

Recommendations and supporting evidence	Strength of recommendations and level of evidence
against severe hypoglycemia in this population." (p. 523)	
Supporting evidence: Older persons with diabetes were at a significantly higher risk for severe hypoglycemia than younger individuals. Investigations in the use of CGM within this population have been shown to detect and reduce hypoglycemia, reduce hemoglobin A1C, and improve QoL.	
In a 2020 RCT, 203 older adults (≥ 60 years) were randomized to use CGM or SMBG. At 6 months, CGM was associated with a decrease in severe hypoglycemia compared with SMBG, showing statistically significant reductions in severe hypoglycemia incidence rates compared with SMBG. The use of CGM was also associated with reductions in the percentage of time spent < 70 mg/dL versus increases with SMBG use.	
The investigators of a subgroup analysis of T1D and T2D trial cohorts assessed changes in glycemic status among rtCGM versus SMBG users and reported statistically significant hemoglobin A1C reduction with rtCGM versus SMBG use.	
Diabetes Canada, 2021[27]	
Blood glucose monitoring in adults and children with diabetes	**Strength of recommendation:** i, ii – Grade A (best evidence was Level 1)
Recommendation 5: In individuals with type 1 diabetes using basal-bolus insulin therapy or CSII, who are willing and able to use these devices on a nearly daily basis:	iii, iv – Grade B (best evidence was Level 2)
rtCGM should be used to:	**Level of evidence:**
i – reduce hemoglobin A1C and increase TIR	i, ii – 1A (SR or MA of high-quality RCTs, or appropriately designed RCT with adequate power)
ii – reduce duration and incidence of hypoglycemia	iii, iv – 2 (low-quality RCT or systematic overview)
iii – improve aspects of diabetes-specific quality of life (in adults)	
iv – increase treatment satisfaction (in adults using CSII). (p. 584)	
Supporting evidence: For people living with T1D who use basal-bolus injection therapy or CSII, rtCGM has been shown to reduce hemoglobin A1C and increase glucose TIR, while simultaneously reducing duration and incidence of hypoglycemia in adults and children. These glycemic benefits of rtCGM have been demonstrated in trials recruiting adults and children with hemoglobin A1C at target (< 7.5%) or above target; and in trials which included adults at or above target. rtCGM has been shown to reduce biochemical (i.e., not necessarily symptomatic) hypoglycemia in adults. rtCGM has also been shown to improve quality of life and hypoglycemia distress in adults with T1D.	
Two of 3 RCTs that included children as young as 6 years, comparing rtCGM to CBG testing, showed lower hemoglobin A1C and less TBR in both adults and children, but this was not seen in pediatric participants in the other study, which had very low use of rtCGM and was under-powered to detect differences in hypoglycemia. Lower hemoglobin A1C with rtCGM in children may depend on time spent using CGM since further analysis of pediatric subjects in this latter trial showed use of rtCGM for 6 or more days per week improved hemoglobin A1C by −0.8% at 12 months. Characteristics such as younger age, and higher frequency of CBG testing prior to rtCGM, may help predict those who	

Recommendations and supporting evidence	Strength of recommendations and level of evidence
are more likely to use rtCGM consistently. Another study in younger children (ages 4 to 10 years) did not show any change or differences in hemoglobin A1C or CGM parameters between groups, although the use of rtCGM was associated with a high degree of parental satisfaction with rtCGM. These findings underscore a fear of hypoglycemia, which is reflected in more conservative recommended glucose targets.	
Recommendation 6: In adults with type 1 diabetes with impaired awareness of hypoglycemia or recent severe hypoglycemia: a – rtCGM should be used to reduce incidence of hypoglycemia and severe hypoglycemic events compared with CBG testing b – rtCGM is recommended to reduce time in hypoglycemia compared with isCGM. (p. 584) **Supporting evidence:** rtCGM has been shown to reduce episodes of severe hypoglycemia in adults with a history of severe hypoglycemia or impaired awareness of hypoglycemia using MDI. Two studies have directly compared rtCGM with isCGM in adults with T1D. rtCGM users spent more TIR and less time below range than isCGM users in a 5-week RCT in adults with normal awareness of hypoglycemia using MDI or CSII. In an 8-week study of individuals with impaired awareness of, or recent severe hypoglycemia using MDI, rtCGM reduced time in hypoglycemia and fear of hypoglycemia, which was not seen with isCGM. Superiority of rtCGM to protect from hypoglycemia in this high-risk population was supported in the extension phase of this study, where switching to rtCGM was associated with significant reduction in TBR in subjects originally randomized to isCGM.	**Strength of recommendation:** a – Grade A b – Grade B **Quality of evidence:** a – 1A b – 2
Recommendation 7: In adults with type 2 diabetes using basal-bolus insulin therapy who have not achieved their hemoglobin A1C target, who are willing and able to use these devices on a nearly daily basis: • rtCGM may be used to reduce A1C and duration of hypoglycemia. (p. 584) **Supporting evidence:** For people living with T2D using basal-bolus injection therapy, a randomized controlled trial of 158 subjects demonstrated that the use of rtCGM reduced hemoglobin A1C to a greater extent than usual care, with more time spent in the target range and less time spent above range at 24 weeks.	**Strength of recommendation:** Grade A **Quality of evidence:** 1A

AACE = American Association of Clinical Endocrinology; ADA = American Diabetes Association; CBG = capillary blood glucose; CGM = continuous glucose monitoring; CSII = continuous subcutaneous insulin infusion; isCGM = intermittently scanned continuous glucose monitoring; MA = meta-analysis; MDI = multiple daily injection; NICE = National Institute for Health and Care Excellence; NR = not reported; QoL = quality of life; RCT = randomized controlled trial; rtCGM, real-time continuous glucose monitoring; SMBG = self-monitoring of blood glucose; SR = systematic review; T1D = type 1 diabetes; T2D = type 2 diabetes; TBR = time below range; TIR = time in range.

Appendix 5: References of Potential Interest

Note that this appendix has not been copy-edited.

Previous CADTH Reports

Intermittently Scanned and Real-Time Continuous Glucose Monitoring for People with Diabetes. Ottawa (ON): CADTH. 2022 https://www.cadth.ca/intermittently-scanned-and-real-time-continuous-glucose-monitoring-people-diabetes

Flash Glucose Monitoring and Continuous Glucose Monitoring for People with Diabetes in Acute Care Settings. Ottawa (ON): CADTH. 2021 https://www.cadth.ca/flash-glucose-monitoring-and-continuous-glucose-monitoring-people-diabetes-acute-care-settings

Continuous Glucose Monitoring for Patients with All Diabetes Types: Clinical Effectiveness and Guidelines. Ottawa (ON): CADTH. 2018 https://www.cadth.ca/continuous-glucose-monitoring-patients-all-diabetes-types-clinical-effectiveness-and-guidelines

Self-Monitoring of Blood Glucose Frequency for Patients with Hypoglycemia Unawareness: A Review of Clinical Effectiveness and Guidelines. Ottawa (ON): CADTH. 2017 https://www.cadth.ca/self-monitoring-blood-glucose-frequency-patients-hypoglycemia-unawareness-review-clinical

Other Guideline Documents

Borot S, Benhamou PY, Atlan C, et al. Practical implementation, education and interpretation guidelines for continuous glucose monitoring: A French position statement. *Diabetes Metab*. 2018;44(1):61-72. PubMed

Danne T, Nimri R, Battelino T, et al. International Consensus on Use of Continuous Glucose Monitoring. *Diabetes Care*. 2017;40(12):1631-1640. PubMed

Kesavadev J, Misra A, Saboo B, et al. Time-in-range and frequency of continuous glucose monitoring: Recommendations for South Asia. *Diabetes Metab Syndr*. 2022;16(1):102345. PubMed

Petrie JR, Peters AL, Bergenstal RM, Holl RW, Fleming GA, Heinemann L. Improving the Clinical Value and Utility of CGM Systems: Issues and Recommendations: A Joint Statement of the European Association for the Study of Diabetes and the American Diabetes Association Diabetes Technology Working Group. *Diabetes Care*. 2017;40(12):1614-1621. PubMed

Guideline Documents, Methodology Not Reported

Borot S, Benhamou PY, Atlan C, et al. Practical implementation, education, and interpretation guidelines for continuous glucose monitoring: A French position statement. *Diabetes Metab*. 2018;44(1):61-72. PubMed

Review Articles

Pettus J, Edelman SV. Recommendations for Using Real-Time Continuous Glucose Monitoring (rtCGM) Data for Insulin Adjustments in Type 1 Diabetes. *J Diabetes Sci Technol*. 2017;11(1):138-147. PubMed

Ziegler R, von Sengbusch S, Kroger J, et al. Therapy Adjustments Based on Trend Arrows Using Continuous Glucose Monitoring Systems. *J Diabetes Sci Technol*. 2019;13(4):763-773. PubMed

Additional Reference

Bruttomesso D, Laviola L, Avogaro A, et al. The use of real time continuous glucose monitoring or flash glucose monitoring in the management of diabetes: A consensus view of Italian diabetes experts using the Delphi method. *Nutrition, Metabolism and Cardiovascular Diseases*. 2019;29(5):421-431. PubMed