TEXAS CHILDREN'S HOSPITAL
EVIDENCE-BASED OUTCOMES CENTER
Continuous Glucose Monitoring in Pediatric Type 1 Diabetes Mellitus Patients
Evidence Summary

Inclusion Criteria
- Children (<18 years of age) with type 1 diabetes mellitus

Exclusion Criteria
- Adults (>18 years of age)
- Type 2 diabetes

Critically Analyze the Evidence

The **GRADE criteria** were used to evaluate the quality of evidence presented in research articles reviewed during the development of this guideline. The table below defines how the quality of evidence is rated and how a strong versus a weak recommendation is established.

Recommendation	
STRONG	Desirable effects clearly outweigh undesirable effects or vice versa
WEAK	Desirable effects closely balanced with undesirable effects
Quality	**Type of Evidence**
High	Consistent evidence from well-performed RCTs or exceptionally strong evidence from unbiased observational studies
Moderate	Evidence from RCTs with important limitations (e.g., inconsistent results, methodological flaws, indirect evidence, or imprecise results) or unusually strong evidence from unbiased observational studies
Low	Evidence for at least 1 critical outcome from observational studies, from RCTs with serious flaws or indirect evidence
Very Low	Evidence for at least 1 critical outcome from unsystematic clinical observations or very indirect evidence

PICO Question 1: In pediatric patients with type 1 diabetes mellitus (T1DM), does continuous glucose monitoring (CGM), when compared to conventional self-monitoring of blood glucose (SMBG) levels improve glycemic control, reduce hypoglycemic events, reduce preventable hospital admissions or readmissions, and/or demonstrate cost effectiveness?

Recommendation(s): Strong recommendation with **moderate quality evidence** to offer continuous glucose monitoring (CGM) to children with type 1 diabetes mellitus regardless of race, gender, or insurance type who have the following. [1-15]
- Frequent episodes of mild hypoglycemia, OR
- A single episode of severe hypoglycemia, OR
- Impaired awareness of hypoglycemia, OR
- Inability to recognize or communicate symptoms of hypoglycemia, OR
- Children and young people who undertake high levels of physical activity, OR
- HbA1c >7.5% as a useful tool to achieve the HbA1c goal, OR
- HbA1c ≤ 7.5% to assist in maintaining target HbA1c levels while limiting the risk of hypoglycemia.

Continuous glucose monitoring has been used as a tool to give the patient and the multidisciplinary team real-time information about glucose levels. This sensor, placed subcutaneously, can be used to generate reports of glucose levels and in many devices, provide real-time display of information.
Fourteen studies were identified that reviewed glycemic control (hemoglobin A1C). Four meta-analyses analyzed the effect of continuous glucose monitoring (CGM) vs. self-monitoring of blood glucose (SMBG), and looked at both retrospective and real time devices.[1-4] In pooled estimates, many of the studies demonstrated statistically significant differences in glycemic control in favor of CGM devices [1,3,4] with a more pronounced decrease when real-time CGM devices were used compared to retrospective devices [1,3] although one meta-analysis found that this was not statistically significant in subgroup analysis on adolescents. [2] In one randomized controlled trial (RCT) that reported on sensor-augmented pump therapy (SAP) [5] children and adolescents showed improved hemoglobin A1c (HbA1c) values by three months. Children (7-12 years) maintained those improved values throughout the study, but this was not maintained in adolescents (13-18 years). Of the ten observational studies that looked at HbA1c [6-14], four showed improvement in glycemic control [7,9,10,14], five showed improvement in groups with consistent use [6,8,11,12,14], and one failed to show

statistically significant changes in HbA1c [13] but had a very small sample size and methodological limitations. In age group comparisons, two studies [11,14] showed limited effectiveness when looking at adolescents.
A total of nine studies reported on hypoglycemic events, including three meta-analyses [1,2,,4] and six observational studies. [6-8,11,12,14] Six studies reported events of severe hypoglycemia (defined as an event that required assistance from another person to administer carbohydrate, glucagon, or other resuscitative actions) and found no statistically significant differences in rates of severe hypoglycemia when comparing CGM vs. SMBG groups, but did note that those events were rare in the study period for both groups. [2,4,7,8,11,12,14] One meta-analysis [1] reported a decreased duration of hypoglycemia in the CGM group compared to the SMBG group, and an observational study [6] demonstrated a statistically significant reduction in the incidence of hypoglycemia in favor of the CGM group.
Three studies, one meta-analysis [2] and two observational studies [12,14] reported on admissions or re-admissions attributed to diabetes, but none showed statistically significant differences between CGM and SMBG groups since hospital admissions were a rare event during the study period.
Only one study reported on cost-effectiveness and found that CGM was projected to gain 0.6 quality-adjusted life year compared to SMBG groups for those with HbA1c ≥ 7%, and 1.11 QALY for those with HbA1c <7%.[15] These calculations were made under the assumption that the unit cost of the device and sensors reflected full retail prices with no insurer discount, although the authors did report that if test strip use had been two per day, the incremental cost effectiveness ratio for CGM would improve significantly. With future technology advancements, if devices improve and the requirement to calibrate with SMBG devices is no longer required, the cost-effectiveness of CGM devices will increase significantly.

Critical Points of Evidence*

Evidence Supports

- Continuous glucose monitoring should be offered to patients regardless of race, gender, or insurance type who have the following. [1-15] – Strong recommendation, moderate quality evidence
    - Frequent episodes of mild hypoglycemia, OR
    - A single episode of severe hypoglycemia, OR
    - Impaired awareness of hypoglycemia, OR
    - Inability to recognize or communicate symptoms of hypoglycemia, OR
    - Children and young people who undertake high levels of physical activity, OR
    - HbA1c >7.5% as a useful tool to achieve the HbA1c goal, OR
    - HbA1c ≤ 7.5% to assist in maintaining target HbA1c levels while limiting the risk of hypoglycemia.

- The provider should stress to the patients and families that the best outcomes are seen in patients who use the device at least 6 days a week.
- The multidisciplinary team should offer education and support to the patients and families and to help identify potential barriers to adherence.

*NOTE: The references cited represent the entire body of evidence reviewed to make each recommendation.

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Clinical Standards Preparation

This clinical standard was prepared by the Evidence-Based Outcomes Center (EBOC) team in collaboration with content experts at Texas Children's Hospital. Development of this clinical standard supports the TCH Quality and Patient Safety Program initiative to promote clinical standards and outcomes that build a culture of quality and safety within the organization.

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No relevant financial or intellectual conflicts to report.

Development Process

This clinical standard was developed using the process outlined in the EBOC Manual. The literature appraisal documents the following steps:

1. Review Preparation
   - PICO questions established
   - Evidence search confirmed with content experts
2. Review of Existing External Guidelines
   - Continuous Glucose Monitoring: An Endocrine Society Clinical Practice Guideline
   - Glycemic targets; Standards of Medical Care in Diabetes
   - Outpatient Continuous Glucose Monitoring Consensus Statement
   - Diabetes (type 1 and type 2) in children and young people: diagnosis and management.
3. Literature Review of Relevant Evidence
   - Searched: PubMed, Cochrane
4. Critically Analyze the Evidence
5. Summarize the Evidence
   - Materials used in the development of the clinical standard, literature appraisal, and any order sets are maintained in a Continuous Glucose Monitoring in Pediatric Type 1 Diabetes Mellitus Patients evidence-based review manual within EBOC.

Evaluating the Quality of the Evidence

Published clinical guidelines were evaluated for this review using the **AGREE II** criteria. The summary of these guidelines are included in the literature appraisal. AGREE II criteria evaluate Guideline Scope and Purpose, Stakeholder Involvement, Rigor of Development, Clarity and Presentation, Applicability, and Editorial Independence using a 4-point Likert scale. The higher the score, the more comprehensive the guideline.
This clinical standard specifically summarizes the evidence *in support of* or *against* specific interventions and identifies where evidence is *lacking/inconclusive*. The following categories describe how research findings provide support for treatment interventions.

"Evidence Supports" provides evidence to support an intervention
"Evidence Against" provides evidence against an intervention.
"Evidence Lacking/Inconclusive" indicates there is insufficient evidence to support or refute an intervention and no conclusion can be drawn *from the evidence.*
The **GRADE** criteria were utilized to evaluate the body of evidence used to make practice recommendations. The table below defines how the quality of the evidence is rated and how a strong versus weak recommendation is established. The literature appraisal reflects the critical points of evidence.

Recommendation	
STRONG	Desirable effects clearly outweigh undesirable effects or vice versa
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Recommendations

Practice recommendations were directed by the existing evidence and consensus amongst the content experts. Patient and family preferences were included when possible. The Content Expert Team and EBOC team remain aware of the controversies in the diagnosis/management of a Continuous Glucose Monitoring in Pediatric Type 1 Diabetes Mellitus Patients in children. When evidence is lacking, options in care are provided in the clinical standard and the accompanying order sets (if applicable).

Approval Process

Clinical standards are reviewed and approved by hospital committees as deemed appropriate for its intended use. Clinical standards are reviewed as necessary within EBOC at Texas Children's Hospital. Content Expert Teams are involved with every review and update.

Disclaimer

Practice recommendations are based upon the evidence available at the time the clinical standard was developed. Clinical standards (guidelines, summaries, or pathways) do not set out the standard of care and are not intended to be used to dictate a course of care. Each physician/practitioner must use his or her independent judgment in the management of any specific patient and is responsible, in consultation with the patient and/or the patient's family, to make the ultimate judgment regarding care.

Version History

Date	Comments
November 2016	Originally completed
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