1.01.20	Continuous Glucose Monitoring		
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Policy Statement

I. Continuous glucose monitoring (CGM) of glucose levels in interstitial fluid, as a technique of diabetic monitoring, may be considered **medically necessary** when **both** of the following situations occur:
   A. Individuals with insulin dependent (type 1 or type 2) diabetes requiring multiple (three or more) daily doses of insulin
   B. The device includes an audible or tactile (vibrating) alarm for low glucose alerts without patient intervention
   (NOTE: the FreeStyle Libre 14 day device does not have alarms but the FreeStyle Libre 2 does have appropriate alarms, as do Dexcom G5 and G6)

II. The use of implantable CGM devices (e.g., Eversense®) for management of Type 1 and Type 2 diabetes mellitus is considered **investigational** (see Policy Guidelines section).

III. The use of continuous noninvasive glucose monitoring devices (see Policy Guidelines section) are considered **investigational.**

IV. Other uses of long-term CGM of glucose levels as a technique of diabetic monitoring in individuals who are not insulin dependent (including use in gestational diabetes) are considered **investigational**.

NOTE: Refer to Appendix A to see the policy statement changes (if any) from the previous version.

Policy Guidelines

This policy only evaluates continuous (real time or intermittently scanned) interstitial glucose monitors and does not evaluate the use of continuous glucose monitoring that is integrated into insulin pumps.

Supplies needed for continuous glucose monitoring such as disposable sensors or transmitters are not covered for individuals who do not meet the criteria for CGM.

Continuous Glucose Monitors
A separate monitor device was needed in the past but now there are options for phone apps that can be used instead of the monitor. Approval would include either the app or the monitor (receiver) device.

Adjunctive/non-therapeutic and non-adjunctive/therapeutic
Devices that do not require separate fingerstick glucose checks to make treatment decisions are considered to be "therapeutic" or "non-adjunctive". Those that do require separate fingerstick glucose checks to confirm calibration and before making treatment decisions are "adjunctive" or "non-therapeutic" (meaning they are adjuncts or add-ons to fingersticks but not independent of them).

- Adjunctive examples: Guardian Connect by Medtronic
- Non-adjunctive examples: Dexcom G5 / G6 and G7; Freestyle Libre 14 day and 2; Eversense (implantable)

Real time (rtCGM) devices automatically record and store data continuously with no manual intervention needed. Examples include but are not limited to Dexcom G6/G7 and Guardian Connect, both of which also include alarm systems.

Intermittently scanned or flash devices
Intermittently scanned devices (flash CGM or isCGM) require manually bringing the monitor physically close to the sensor to record and display current data (thus, intermittent based on how often the levels are checked/recorded). Examples include but are not limited to the Freestyle Libre 2 which has both alarms and the ability to store data for 8 hours; but data can be lost if not recorded for more than 8 hours. The Freestyle Libre 14 day (original version) does not have alarm capability.

Implantable CGM devices (e.g., Eversense) are small and inserted under the skin through a small incision, then removed and replaced with a new device in another location every 90 days (a newer XL version is implanted every 180 days instead).

Continuous noninvasive devices are often worn like a watch, with a skin patch or with a fingerprint type device and have special sensors that do not require the tiny subcutaneous catheters used with traditional CGMs. Without breaking the skin, this sensor measures the individual's blood sugar levels.

Disposable durable medical equipment (DME) supplies such as sensors and transmitters are considered a covered benefit when the CGM device or app has also been approved. Blue Shield of California (BSC) plans exclude coverage of supplies for units purchased by the individual without prior authorization. Please check benefit plan descriptions for details.

Best practices in diabetes control include compliance with a self-monitoring blood glucose regimen of four or more fingersticks each day and use of an insulin pump or multiple daily injections of insulin. During pregnancy, three or more insulin injections daily could also be considered best practice for individuals not on an insulin pump prior to the pregnancy. Prior short-term (72-hour) use of an intermittent glucose monitor would be considered a part of best practices for those considering long-term use of a continuous glucose monitor. Individuals with type 1 diabetes taking insulin who are pregnant or about to become pregnant with poorly controlled diabetes are another subset of patients that might require either short or long term continuous glucose monitoring.

Significant hypoglycemia may include recurrent, unexplained, severe (generally blood glucose levels less than 50 mg/dL) hypoglycemia or impaired awareness of hypoglycemia that puts the individual or others at risk. When this happens at night while the individual is asleep, the alarm functions are even more important.

Individuals with type 1 diabetes taking insulin who are pregnant or about to become pregnant with poorly controlled diabetes are another subset of individuals to whom the policy statement on short-term continuous glucose monitoring may apply.

The strongest evidence exists for use of continuous glucose monitoring (CGM) devices in individuals age 25 years and older. However, age may be a proxy for motivation and good control of disease, so it is also reasonable to select patients based on their ability to self-manage their disease, rather than their age. Most continuous glucose monitoring (CGM) devices have U.S. Food and Drug Administration labeling related to age.

Providers board-certified in endocrinology and/or providers with a focus on the practice of diabetes care may be considered qualified to evaluate and oversee individuals for continuous (i.e., long-term) monitoring.

Coding

The language of the CPT codes that specifically described monitoring of glucose levels in the interstitial fluid using implanted devices was revised to state that the devices are used for a minimum of 72 hours:

- **95250**: Ambulatory continuous glucose monitoring of interstitial tissue fluid via a subcutaneous sensor for a minimum of 72 hours; physician or other qualified health care professional (office) provided equipment, sensor placement, hook-up, calibration of monitor, patient training, removal of sensor, and printout of recording
- **95251**: Ambulatory continuous glucose monitoring of interstitial tissue fluid via a subcutaneous sensor for a minimum of 72 hours; analysis, interpretation and report

The following CPT code specifically describes glucose monitoring on equipment provided by the patient:

- **95249**: Ambulatory continuous glucose monitoring of interstitial tissue fluid via a subcutaneous sensor for a minimum of 72 hours; patient-provided equipment, sensor placement, hook-up, calibration of monitor, patient training, and printout of recording

CPT code 99091 might also be used for this monitoring:

- **99091:** Collection and interpretation of physiologic data (e.g., ECG, blood pressure, glucose monitoring) digitally stored and/or transmitted by the patient and/or caregiver to the physician or other qualified health care professional, qualified by education, training, licensure/regulation (when applicable) requiring a minimum of 30 minutes of time, each 30 days

The Centers for Medicare & Medicaid created 2 HCPCS codes specific to the use of devices that cannot be used to make treatment decisions (adjunctive or non-therapeutic) (see Continuous Glucose Monitors section above in Guidelines):

- **A4238**: Supply allowance for adjunctive, nonimplanted continuous glucose monitor (CGM), includes all supplies and accessories, 1 month supply = 1 unit of service ***(Code revision effective 1/1/2023)***
- **E2102**: Adjunctive, nonimplanted continuous glucose monitor (CGM) or receiver***(Code revision effective 1/1/2023)***

Effective January 1, 2023, there are new HCPCS codes that expanded the classification of DME to a larger group of CGMs regardless of whether the CGMs are non-adjunctive (can alert patients when glucose levels are approaching dangerous levels, including while they sleep and also replace blood glucose monitors) or adjunctive (can alert patients when glucose levels are approaching dangerous levels, including while they sleep but do not replace blood glucose monitors), as long as the CGMs satisfy the regulatory definition of DME.

- **A4239**: Supply allowance for nonadjunctive, nonimplanted continuous glucose monitor (CGM), includes all supplies and accessories, 1 month supply = 1 unit of service
- **E2103**: Nonadjunctive, nonimplanted continuous glucose monitor (CGM) or receiver

The following non-specific HCPCS codes have been deleted by CMS but are still available for use otherwise for continuous glucose monitoring systems. These are non-specific related to adjunctive and non-adjunctive, so CMS prefers the use of the new codes (A4238 and E2102) that are more specific:

- **A9276**: Sensor; invasive (e.g., subcutaneous), disposable, for use with nondurable medical equipment interstitial continuous glucose monitoring system (CGM), one unit = 1 day supply ***(Code revision effective 1/1/2023)***
- **A9277**: Transmitter; external, for use with nondurable medical equipment interstitial continuous glucose monitoring system (CGM) ***(Code revision effective 1/1/2023)***

Effective January 1, 2023, the following HCPCS has been **deleted**:

- **G0308**: Creation of subcutaneous pocket with insertion of 180 day implantable interstitial glucose sensor, including system activation and patient training
- **G0309**: Removal of implantable interstitial glucose sensor with creation of subcutaneous pocket at different anatomic site and insertion of new 180 day implantable sensor, including system activation
- **K0553**: Supply allowance for therapeutic continuous glucose monitor (CGM), includes all supplies and accessories, 1 month supply = 1 unit of service
- **K0554**: Receiver (monitor), dedicated, for use with therapeutic glucose continuous monitor system

Description

Tight glucose control in patients with diabetes has been associated with improved health outcomes. Several devices are available to measure glucose levels automatically and frequently (e.g., every 5 to 10 minutes). The devices measure glucose in the interstitial fluid and are approved as adjuncts to or replacements for traditional self-monitoring of blood glucose levels. Devices can be used on a long-term (continuous) or short-term (often referred to as intermittent) basis.

Related Policies

- N/A

Benefit Application

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

Some state or federal mandates (e.g., Federal Employee Program [FEP]) prohibits plans from denying Food and Drug Administration (FDA)-approved technologies as investigational. In these instances, plans may have to consider the coverage eligibility of FDA-approved technologies on the basis of medical necessity alone.

Regulatory Status

Multiple CGM systems have been approved or cleared by the FDA (see Table 1). FDA product codes: [PMA] QCD, MDS, PQF; [510(k)] QBJ, QLG.

CGM devices labeled as “Pro” for specific professional use with customized software and transmission to health care professionals are not enumerated in this list.

The Flash glucose monitors (e.g. FreeStyle Libre, Abbott) use intermittent scanning. The current version of the FreeStyle Libre device includes real-time alerts, in contrast to earlier versions without this feature.

Table 1. CGM Systems Approved by the U.S. Food and Drug Administration

Device	Manufacturer	Approval or Clearance	Indications
Continuous Glucose	MiniMed	1999	3-d use in physician's office

Device	Manufacturer	Approval or Clearance	Indications
Monitoring System (CGMS®)			
GlucoWatch G2® Biographer		2001	Not available since 2008
Guardian®-RT (Real-Time) CGMS	MiniMed (now Medtronic)	2005	
Dexcom® STS CGMS system	Dexcom	2006	
Paradigm® REAL-Time System (second-generation called Paradigm Revel System)	MiniMed (now Medtronic)	2006	Integrates CGM with a Paradigm insulin pump
FreeStyle Navigator® CGM System	Abbott	2008	
Dexcom® G4 Platinum	Dexcom	2012	Adults ≥18 y; can be worn for up to 7 d
		2014	Expanded to include patients with diabetes 2-17 y
Dexcom® G5 Mobile CGM	Dexcom	2016[a]	Replacement for fingerstick blood glucose testing in patients ≥2 y. System requires at least 2 daily fingerstick tests for calibration purposes, but additional fingersticks are not necessary because treatment decisions can be made based on device readings[4,]
Dexcom® G6 Continuous Glucose Monitoring System	Dexcom	2018	Children, adolescents, and adults ≥ 2 years; indicated for the management of diabetes in persons age ≥2 years. Intended to replace fingerstick blood glucose testing for diabetes treatment decisions. Intended to autonomously communicate with digitally connected devices, including automated insulin dosing (AID) systems with 10-day wear
Freestyle Libre®Flash Glucose Monitoring System	Abbott	2017	Adults ≥18 y. Indicated for the management of diabetes and can be worn up to 10 days It is designed to replace blood glucose testing for diabetes treatment decisions.
Freestyle Libre® Flash Glucose Monitoring System	Abbott	2018	Adults ≥18 y. Extended duration of use to 14 days
Freestyle Libre® 2 Flash Glucose Monitoring System	Abbott	2020	Children, adolescents, and adults ≥2 years, including pregnant women
Guardian Connect	Medtronic MiniMed	2018	Adolescents and adults (14-75 years) Continuous or periodic monitoring of interstitial glucose levels. Provides real-time glucose values, trends, and alerts through a Guardian Connect app installed on a compatible consumer electronic mobile device
Eversense Continuous Glucose Monitoring System	Senseonics	2018/2019	Adults ≥18 y. Continually measuring glucose levels up to 90 days. Use as an adjunctive device to complement, not replace, information obtained from standard home blood glucose monitoring devices. Adults ≥18 y. Continually measuring glucose levels up to 90 days. Indicated for use to replace fingerstick blood glucose measurements for diabetes

Device	Manufacturer	Approval or Clearance	Indications
			treatment decisions. Historical data from the system can be interpreted to aid in providing therapy adjustments.
Eversense E3 Continuous Glucose Monitoring System	Senseonics	2022	Adults ≥18 y. Continually measuring glucose levels up to 180 days. The system is indicated for use to replace fingerstick blood glucose measurements for diabetes treatment decisions. The system is intended to provide real-time glucose readings, provide glucose trend information, and provide alerts for the detection and prediction of episodes of low blood glucose (hypoglycemia) and high blood glucose (hyperglycemia). The system is a prescription device. Historical data from the system can be interpreted to aid in providing therapy adjustments. These adjustments should be based on patterns and trends seen over time.
FreeStyle Libre® 3 Continuous Glucose Monitoring System	Abbott	2022	Children, adolescents, and adults ≥2 years, including pregnant women
Dexcom® G7 Continuous Glucose Monitoring System	Dexcom	2022	Children, adolescents, and adults ≥2 years

CGM: continuous glucose monitoring.
[a] As a supplement to the G4 premarketing approval.

Rationale

Background

Blood Glucose Control

The advent of blood glucose monitors for use by patients in the home revolutionized the management of diabetes. Using fingersticks, patients can monitor their blood glucose levels both to determine the adequacy of hyperglycemia control and to evaluate hypoglycemic episodes. Tight glucose control, defined as a strategy involving frequent glucose checks and a target hemoglobin A_{1c} (HbA1c) level in the range of 7%, is now considered the standard of care for patients with diabetes. Randomized controlled trials assessing tight control have demonstrated benefits for patients with type 1 diabetes in decreasing microvascular complications. The impact of tight control on type 1 diabetes and macrovascular complications such as stroke or myocardial infarction is less certain. The Diabetes Control and Complications Trial (2002) demonstrated that a relative HbA1c level reduction of 10% is clinically meaningful and corresponds to approximately a 40% decrease in risk for progression of diabetic retinopathy and a 25% decrease in risk for progression of renal disease.[1,]

Due to an increase in turnover of red blood cells during pregnancy, HbA1c levels are slightly lower in women with a normal pregnancy compared with nonpregnant women. The target HbA1cin women with diabetes is also lower in pregnancy. The American Diabetes Association recommends that, if achievable without significant hypoglycemia, the HbA1clevels should range between 6.0% to 6.5%; an HbA1clevel less than 6% may be optimal as the pregnancy progresses.[2,]

Tight glucose control requires multiple daily measurements of blood glucose (i.e., before meals and at bedtime), a commitment that some patients may find difficult to meet. The goal of tight glucose control has to be balanced with an associated risk of hypoglycemia. Hypoglycemia is known to be a risk in patients with type 1 diabetes. While patients with insulin-treated type 2 diabetes may also experience severe hypoglycemic episodes, there is a lower relative likelihood of severe hypoglycemia compared with patients who had type 1 diabetes.[3,] An additional limitation of periodic self-

measurements of blood glucose is that glucose levels are seen in isolation, and trends in glucose levels are undetected. For example, while a diabetic patient's fasting blood glucose level might be within normal values, hyperglycemia might be undetected postprandially, leading to elevated HbA1c levels.

Management

Measurements of glucose in the interstitial fluid have been developed as a technique to measure glucose values automatically throughout the day, producing data that show the trends in glucose levels. Although devices measure glucose in the interstitial fluid on a periodic rather than a continuous basis, this type of monitoring is referred to as continuous glucose monitoring (CGM).

Currently, CGM devices are of 2 designs; real-time CGM (rtCGM) provides real-time data on glucose level, glucose trends, direction, and rate of change, and intermittently viewed (iCGM) devices that show continuous glucose measurements retrospectively. These devices are also known as flash-glucose monitors.

Approved devices now include devices indicated for pediatric use and those with more advanced software, more frequent measurements of glucose levels, or more sophisticated alarm systems. Devices initially measured interstitial glucose every 5 to10 minutes and stored data for download and retrospective evaluation by a clinician. With currently available devices, the intervals at which interstitial glucose is measured range from every 1 to 2 minutes to 5 minutes, and most provide measurements in real-time directly to patients. While CGM potentially eliminates or decreases the number of required daily fingersticks, according to the U.S. Food and Drug Administration (FDA) labeling, some marketed monitors are not intended as an alternative to traditional self-monitoring of blood glucose levels but rather as adjuncts to monitoring, supplying additional information on glucose trends not available from self-monitoring while other devices are factory calibrated and do not require fingerstick blood glucose calibration.

Devices may be used intermittently (i.e., for periods of 72 hours) or continuously (i.e., on a long-term basis).

Literature Review

Evidence reviews assess the clinical evidence to determine whether the use of technology improves the net health outcome. Broadly defined, health outcomes are the length of life, quality of life (QOL), and ability to function, including benefits and harms. Every clinical condition has specific outcomes that are important to patients and managing the course of that condition. Validated outcome measures are necessary to ascertain whether a condition improves or worsens; and whether the magnitude of that change is clinically significant. The net health outcome is a balance of benefits and harms.

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of technology, 2 domains are examined: the relevance, and quality and credibility. To be relevant, studies must represent one or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial (RCT) is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. RCTs are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

The evidence review focuses on the clinical utility of continuous glucose monitoring (CGM) systems. That is, their ability to provide additional information on glucose levels leads to improved glucose

control, or to reduce the morbidity and mortality associated with clinically significant severe and acute hypoglycemic or hyperglycemic events. Because diabetic control encompasses numerous variables, including the diabetic regimen and patient self-management, RCTs are important to isolate the contribution of interstitial glucose measurements to overall diabetes management. For the evaluation of the clinical utility of CGM, studies would need to use the test as either an adjunct or a replacement to current disease status measures to manage treatment decisions in patients with diabetes. Outcomes would include measures of glucose control, QOL and measures of disease progression. Hemoglobin A1c (HbA1c) has commonly been accepted as a marker of glucose control; more recent studies have also reported time in hyperglycemia, time in hypoglycemia, and time in range as intermediate outcome measures.

Promotion of greater diversity and inclusion in clinical research of historically marginalized groups (e.g., People of Color [African-American, Asian, Black, Latino and Native American]; LGBTQIA (Lesbian, Gay, Bisexual, Transgender, Queer, Intersex, Asexual); Women; and People with Disabilities [Physical and Invisible]) allows policy populations to be more reflective of and findings more applicable to our diverse members. While we also strive to use inclusive language related to these groups in our policies, use of gender-specific nouns (e.g., women, men, sisters, etc.) will continue when reflective of language used in publications describing study populations."

Continuous Glucose Monitoring Devices for Long-Term Use in Type 1 Diabetes

In some parts of the analysis of type 1 diabetes, BCBSA combines discussion of real-time and intermittently scanned glucose monitoring because several systematic reviews provided information relevant to both types of devices.

Clinical Context and Therapy Purpose

The purpose of long-term CGM devices is to provide a testing option that is an alternative to or an improvement on existing testing used in the management of individuals with type 1 diabetes.

The question addressed in this evidence review is: Does long-term use of a CGM device improve the net health outcome for individuals with type 1 diabetes?

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is individuals with type 1 diabetes. All individuals with type 1 diabetes require engagement in a comprehensive self-management and clinical assessment program that includes assessment of blood glucose control.

Interventions

The test being considered is the use of a CGM device to assess blood glucose levels as part of optimal diabetes management. Long-term use is generally use for more than 72 hours.

Currently, CGM devices are of 2 designs; real-time CGM (rtCGM) provides real-time data on glucose level, glucose trends, direction, and rate of change, and intermittently scanned (iCGM) devices that show continuous glucose measurements retrospectively. These latter devices are also known as flash-glucose monitors.

Comparators

The following practice is currently being used to measure glucose levels: capillary blood sampling (finger stick) for self-monitoring of blood glucose (SMBG). Standard treatment for patients with type 1 diabetes includes injection of long-acting basal insulin plus multiple daily injections (MDI) of rapid-acting insulin boluses as required for meal intake. Activity level may require patients need to modify the timing and dose of insulin administration. Individuals with type 1 diabetes may also use an insulin pump either for initial treatment or convert to pump use after a period of MDI. Individuals are

required to check their blood glucose before making preprandial insulin calculations, in response to symptoms of hypoglycemia or related to activity-related insulin adjustments.

Outcomes

The general outcomes of interest are change in HbA1c levels, time spent in hypoglycemia and hyperglycemia, time in range (generally glucose of 70 to 180 mg/dl), the incidence of hypoglycemic events, complications of hypoglycemia, and QOL. To assess short-term outcomes such as HbA1c levels, a minimum follow-up of 8 to 12 weeks is appropriate.

Study Selection

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess long-term outcomes and adverse effects, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded.

Review of Evidence

Systematic Reviews

A number of systematic reviews and meta-analyses have assessed RCTs evaluating CGM for long-term, daily use in treating type 1 diabetes.[5,6,7,8,9,10,] These systematic reviews have focused on slightly different populations, and some did not separate real-time CGM from intermittent glucose monitoring.[8,]

The only analysis to use individual patient data was published by Benkhadra et al (2017).[11,] The meta-analysis evaluated data from 11 RCTs that enrolled patients with type 1 diabetes and compared real-time CGM with a control intervention. Studies in which patients used insulin pumps or received multiple daily insulin injections were included. Reviewers contacted corresponding study authors requesting individual patient data; data were not obtained for 1 trial. Mean baseline HbA1c levels were 8.2% in adults and 8.3% in children and adolescents. The overall risk of bias in the studies was judged to be moderate. In pooled analyses, there was a statistically significantly greater decrease in HbA1c levels with real-time CGM versus control conditions. Overall, the degree of difference between groups was 0.26%. In subgroup analyses by age, there was a significantly greater change in HbA1c levels among individuals 15 years and older, but not among the younger age groups. There were no significant differences between groups in the time spent in hypoglycemia or the incidence of hypoglycemic events. Key findings are shown in Table 2.

Table 2. Individual Patient Data Meta-Analytic Outcomes for Real-Time CGM in Type 1 Diabetes

No. of Trials	N	Group	Point Estimate	95% Confidence Intervals	p
Change in HbA1c levels, %					
8	1371	Overall	-0.258	0.464 to -0.052	.014
7	902	Age >15 y	-0.356	0.551 to -0.160	<.001
7	178	Age 13-15 y	-0.039	-0.320 to 0.242	.787
7	291	Age ≤12 y	-0.047	0.217 to 0.124	.592
Time spent in hypoglycemia <60 mg/dL, min					
4	706	Overall	-8.549	-31.083 to 13 985	.457
4	467	Age >15 y	-8.095	-32.615 to 16.425	.518
3	109	Age 13-15 y	-13.966	31.782 to 3.852	.124
3	130	Age ≤12 y	-9.366	19.898 to 1.167	.081
Incidence of hypoglycemic events <70 mg/dL, mean no. events					
3	351	Overall	0.051	-0.314 to 0.416	.785
3	277	Age >15 y	-0.074	-0.517 to 0.368	.742
2	47	Age 13-15 y	0.536	0.243 to 1.316	.177

No. of Trials	N	Group	Point Estimate	95% Confidence Intervals	p
2	27	Age ≤12 y	0.392	0.070 to 0.854	.097

Adapted from Benkhadra et al (2017).[11,]
CGM: continuous glucose monitoring: HbA1c: hemoglobin A_{1c}.

Randomized Controlled Trials

Recent RCTs are described next and in Tables 3 and 4. HbA1c, blood glucose, event rates, and patient reported outcomes were assessed at 6 months. None of the studies were blinded. The studies had a large number of pre-specified secondary endpoints, and analyses took into consideration the statistical impact of multiple comparisons.

Two 2017 RCTs evaluated long-term, real-time CGM in patients with type 1 diabetes treated with multiple daily insulin injections. Both trials used the Dexcom G4 CGM device. Lind et al (2017) reported on a crossover study with 142 adults ages 18 and older who had baseline HbA1c levels of 7.5% or higher (mean baseline HbA1c level, >8.5%).[12,] Enrolled patients underwent 26-week treatment periods with a CGM device and conventional therapy using SMBG, in random order. There was a 17-week washout period between intervention phases. The primary endpoint was the difference in HbA1c levels at the end of each treatment period. Mean HbA1c levels were 7.9% during CGM use and 8.4% during conventional therapy (MD, -0.4%; p<.01). Treatment satisfaction (measured by the Diabetes Treatment Satisfaction Questionnaire) was significantly higher in the CGM phase than in the conventional treatment phase (p<.001). There was 1 (0.7%) severe hypoglycemic event during the CGM phase and 5 (3.5%) events during conventional therapy. The percentage of time with hypoglycemia (<70 mmol/L) was 2.8% during CGM treatment and 4.8% during conventional therapy.

In the second study, Beck et al (2017) randomized 158 patients on a 2:1 basis to 24 weeks of CGM (n=105) or usual care (n=53).[13,] The primary outcome (change in HbA1c levels at 24 weeks) was 1.0% in the CGM group and 0.4% in the usual care group (p<.001), with a between-group difference of 0.6%. Prespecified secondary outcomes on the proportion of patients below a glycemic threshold at 24 weeks also favored the CGM group. The proportion of patients with HbA1c levels less than 7.0% was 18 (18%) in the CGM group and 2 (4%) in the control group (p=.01). Prespecified secondary outcomes related to hypoglycemia also differed significantly between groups, favoring the CGM group. Comparable numbers for time spent at less than 50 mg/dL were 6 minutes per day in the CGM group and 20 minutes per day in the usual care group (p=.001). The median change in the rate per 24 hours of hypoglycemia events lasting at least 20 minutes at less than 3.0 mmol/L (54 mg/dL) fell by 30% from 0.23 at baseline to 0.16 during follow-up in the CGM group but was practically unchanged (0.31 at baseline and 0.30 at follow-up) in the usual care group (p=.03).[14,]Quality of life measures assessing overall well-being (World Health Organization Well-Being Index), health status (EQ-5D-5L), diabetes distress (Diabetes Distress Scale), hypoglycemic fear (worry subscale of the Hypoglycemia Fear Survey), and hypoglycemic confidence (Hypoglycemic Confidence Scale) have also been reported.[15,] There were no significant differences between CGM and usual care in changes in well-being, health status, or hypoglycemic fear. The CGM group demonstrated a greater increase in hypoglycemic confidence (p=.01) and a greater decrease in diabetes distress (p=.01) than the usual care group.

Two RCTs were published in 2020 that assessed real-time CGM with a Dexcom G5 in adolescents and young adults (Laffel et al, 2020) [16,], and in older adults (Pratley et al, 2020)[17,] Both studies found modest but statistically significant differences in HbA1c between patients who used the CGM devices compared to the control arm at follow-up. Secondary measures of HbA1c and blood glucose were mostly better in the CGM arm. Patient-reported outcome measures were not significantly different between the groups, except that glucose monitoring satisfaction was higher in the adolescents and young adults who used CGM. With the newer technology, patients were able to use a smartphone app to monitor glucose levels.

Two RCTs have evaluated long-term use of intermittently-scanned CGM. Leelarathna et al (2022) reported results of the FLASH-UK (NCT03815006) multicenter RCT including individuals age 16 years and older in the United Kingdom with type 1 diabetes and HbA1c levels between 7.5% and 11.0% who were receiving either continuous subcutaneous insulin infusion or multiple daily injections of insulin.[18,] The trial was conducted from 2019 to 2021 and compared intermittently-scanned CGM (FreeStyle Libre 2; n=78) worn on the arm for 14 days versus usual care with fingerstick testing (n=78). The primary outcome was the HbA1c at 24 weeks. The difference in decrease in HbA1c level at 24 weeks was −0.5% (95% CI, −0.7 to −0.3; p<.001) favoring CGM. The difference in time per day that the glucose level was in target range was 9.0% (95% CI, 4.7 to 13.3) higher or 130 minutes (95% CI, 68 to 192) longer in the CGM group compared to usual care. No participants in the CGM group versus 2 participants in the usual care group had an episode of severe hypoglycemia.

Yan et al (2023) reported results of a multicenter RCT (NCT03522870) conducted in China from 2019 to 2022 comparing intermittently-scanned CGM (FreeStyle Libre; n=54) to capillary blood glucose monitoring (n=50) in adults with sub-optimally controlled type 1 diabetes.[19,] Participants had HbA1c between 7% and 10%. The primary outcome was change in HbA1c at 24 weeks. The mean reduction in the primary outcome in the CGM group was 0.7% versus 0.3% in the control group (difference, 0.3%; 95% CI, 0.0 to 0.6; p=.04). The mean time-in-range increased to 63% at 24 weeks in CGM versus 58% in control (difference, 6% [1.4 hours / day]; 95% CI, -11 to -1; p=.02). No participants in the CGM group versus 4 participants in the control group experienced an event of diabetic ketoacidosis. No participants in either group experienced severe hypoglycemia.

Table 3. Summary of Key RCT Characteristics in Patients with Type 1 Diabetes

Study; Trial	Countries	Sites	Dates	Participants	Interventions	
					CGM	SMBG
Beck et al (2017)[13,] DIAMOND				Adults aged 25 or older with baseline HbA1c levels between 7.5% and 10%	Dexcom G4 real-time CGM (n=105)	Usual care (n=53)
Laffel et al (2020)[16,]	US	14	2018-2019	Adolescents and young adults age 14 to 24 years with HbA1c 7.5% to 10.9% with multiple daily insulin injections or an insulin pump	Dexcom G5 real-time CGM, with training on use and a smartphone app and 2 calibration BG per day (n=74)	Fingerstick blood glucose meter checks at least 4 times daily (n=79)
Pratley et al (2020)[17,](WISDM)	US	22	1993-2012	Older adults ≥ 60 years of age with HbA1c < 10.0% with multiple daily insulin injections or an insulin pump	Dexcom G5 real-time CGM with training on use and 2 calibration BG checks per day (n=103)	Fingerstick blood glucose meter checks at least 4 times daily (n=100)
Leelarathna et al (2022)[18,]	UK	8	2019-2021	Ages16 and older with type 1 diabetes and HbA1c levels between 7.5% and 11.0% who were receiving either continuous subcutaneous insulin infusion or multiple daily injections of insulin; mean age,	FreeStyle Libre 2 intermittently-scanned CGM worn on the arm for 14 days (n=78)	Usual care with fingerstick testing (n=78)

Study; Trial	Countries	Sites	Dates	Participants	Interventions	
				44 yr; mean HbA1c, 8.6%		
Yan et al (2023)[19,]	China	3	2018-2022	Ages 18 and older with type 1 diabetes and HbA1c between 7% and 10% with stable insulin regimen; 64% female; mean age, 34 yr; mean HbA1c, 8.1%	FreeStyle Libre intermittently scanned CGM (n=54)	Fingerstick blood glucose meter checks (n=50)

BG: blood glucose; CGM: continuous glucose monitoring; HbA1c: hemoglobin A1C; RCT: randomized controlled trial; SMBG: self-monitored blood glucose; WISDM: Wireless Innovation for Seniors With Diabetes Mellitus.

Table 4. Summary of Key RCT Results in Patients with Type 1 Diabetes

Study	HbA1c	HbA1c	Blood Glucose (SD) mg/dL	Hypoglycemic Episodes	Patient Reported Outcomes	Patient Reported Outcomes
Beck et al (2017)[13,] DIAMOND	*Change from Baseline*	*Proportion <7.0%*		*Minutes per day <70 mg/dL*		
CGM	1.0%	18 (18%)		43		
SMBG	0.4%	2 (4%)		80		
Diff (95% CI)	0.6%					
p	<.001	.01		.002		
Laffel et al (2020)[16,]	*Change from Baseline*	*Percent with Reduction of 0.5%*	*Mean (SD)*	*Per Week*	*PAD-PS Survey*	*Glucose Monitoring Satisfaction*
CGM	-0.4 (1.0)	44%	199 (36)	1.4 (0.4 to 2.6)		
SMBG	0.1 (0.8)	21%	217 (35)	1.7 (1.0 to 3.1)		
Diff (95% CI)	-0.37 (-0.66 to -0.08)	23% (7% to 37%)	-14.3 (-23.6 to -5.1)	-0.3 (-0.7 to 0.1)	-0.1 (-3.0, 4.0)	0.27 (0.06, 0.54)
p	.01	.005	.003	.11	.73	.003
Pratley et al (2020)[17,](WISDM)	*At follow-up*	*Percentage of time glucose values <70 mg/dL*		*Per week*	*Quality of life*	*Hypoglycemia Awareness*
CGM	7.2 (0.9)	2.7%	162 (23)	0.8 (0.3-2.2)		
SMBG	7.4 (0.9)	4.9%	171 (30)	1.8 (0.7-4.0)		
Diff (95% CI)	-0.3 (-0.4 to -0.1)	-1.9% (-2,8 to -1.1)	−7.7 (−13.1 to −2.4)	−0.9 (−1.3 to −0.5)		
p		<.001	.005	<.001	NS	NS
Leelarathna et al (2022)[18,]	Change from baseline, mean (SD)	Proportion ≤ 7.0%, n (%)	At 24 weeks follow-up	Severe hypoglycemia, n (%)	NR	NR
CGM	-0.8 (0.8)	11 (15)	178 (32)	0 (0)		
SMBG	-0.2 (0.6)	5 (7)	185 (40)	2 (3)		
Diff (95% CI)	-0.5 (-0.7 to -0.3)	OR=2.4 (0.8 to 7.8)	-11 (-20 to 0)	NR		
p	<.001	NR	NR	NR		
Yan et al (2023)[19,]	Change from baseline, mean (SD)				NR	NR

Study	HbA1c	HbA1c	Blood Glucose (SD) mg/dL	Hypoglycemic Episodes	Patient Reported Outcomes	Patient Reported Outcomes
CGM	0.7%		153 (26)	0		
SMBG	0.3%		166 (29)	0		
Diff (95% CI)	0.3% (0.0 to 0.6)		11 (1 to 21)			
p	.04		0.03			

CGM: continuous glucose monitor; CI: confidence interval; HbA1c: hemoglobin A1c; NR: not reported; NS: not significant; PAD-PS; Problem Areas in Diabetes-Pediatric Survey; RCT: randomized controlled trial; SD: standard deviation; SMBG: self monitored blood glucose; WISDM: Wireless Innovation for Seniors With Diabetes Mellitus

Observational Studies

Because several RCTs exist, observational studies will be summarized briefly below only if they capture longer periods of follow-up- (>6 months), larger populations, or particular subgroups of interest.

Long-term follow-up

Observational studies with follow-up of more than 6 months including adults with type 1 diabetes have shown that reductions in acute diabetes events, including severe hypoglycemia and diabetic ketoacidosis are maintained for 1 to 2 years.[20,21,]

Pregnant People

One trial of real-time CGM in pregnant women with type 1 diabetes has been reported. Study characteristics, results, and gaps are summarized here and in Tables 5 to 8. Feig et al (2017) reported results of 2 multicenter RCTs in women ages 18 to 40 with type 1 diabetes who were receiving intensive insulin therapy and who were either pregnant (≤13 weeks and 6 days of gestation) or planning a pregnancy.[22,] The trial enrolling pregnant women is reviewed here. Women were eligible if they had a singleton pregnancy and HbA1c levels between 6.5% and 10.0%. The trial was conducted at 31 hospitals in North America and Europe. Women were randomized to CGM (Guardian REAL-Time or MiniMed Minilink system) plus capillary glucose monitoring or capillary glucose monitoring alone. Women in the CGM group were instructed to use the devices daily. Women in the control group continued their usual method of capillary glucose monitoring. The target glucose range was 3.5 to 7.8 mmol/L and target HbA1c levels were 6.5% or less in both groups. The primary outcome was the difference in change in HbA1c levels from randomization to 34 weeks of gestation. The proportion of completed scheduled study visits was high in both groups; however, participants using CGM had more unscheduled contacts, which were attributed both to sensor issues and to sensor-related diabetes management issues. The median frequency of CGM use was 6.1 days per week (interquartile range, 4.0 to 6.8 d/wk) and 70% of pregnant participants used CGM for more than 75% of the time. The between-group difference in the change in HbA1c levels from baseline to 34 weeks of gestation was statistically significant favoring CGM (MD, -0.19%; 95% CI, -0.34 to -0.03; p=.02). Women in the CGM group spent an increased percentage of time in the recommended glucose control target range at 34 weeks of gestation (68% vs. 61%; p=.003). There were no between-group differences in maternal hypoglycemia, gestational weight gain, or total daily insulin dose. A smaller proportion of infants of mothers in the CGM group were large-for-gestational-age (odds ratio [OR], 0.51; 95% CI, 0.28 to 0.90; p=.02). In addition, for infants of mothers in the CGM group, there were fewer neonatal intensive care admissions lasting more than 24 hours (OR, 0.48; 95% CI, 0.26 to 0.86; p=.02), fewer incidences of neonatal hypoglycemia requiring treatment with intravenous dextrose (OR, 0.45; 0.22 to 0.89; p=.025), and reduced total hospital length stay (3.1 days vs. 4.0 days; p=.0091). Skin reactions occurred in 49 (48%) of 103 CGM participants and 8 (8%) of 104 control participants.

Table 5. RCT Characteristics for Real-Time CGM in Pregnant People With Type 1 Diabetes

Study; Registration	Countries	Sites	Dates	Participants	Interventions	
					Active	Comparator
Feig et al (2017)[22]; NCT01788527	Canada, England, Scotland, Spain, Italy, Ireland, U.S.	31	2013-2016	Pregnant women (<14 wk gestation) with type 1 diabetes receiving intensive insulin therapy with HbA1c levels between 6.5% and 10.0% (mean, 6.9%); mean age, 31 y	CGM (real-time) (n=108)	SMBG (n=107)

CGM: continuous glucose monitoring: HbA1c: hemoglobin A_{1c}; NCT: national clinical trial; RCT: randomized controlled trial; SMBG: self-monitored blood glucose.

Table 6. RCT Outcomes for Real-Time CGM in Pregnant People With Type 1 Diabetes

Study	Infant Large-for-Gestational Age	Gestational Age at Delivery, wk	Severe Hypoglycemia	Caesarean Section	Maternal HbA1c Levels: Change From Baseline to 34 Wk of Gestation	Severe Hypoglycemia
Feig et al (2017)[22],						
N	211	201	200	202	173	214
CGM	53 (53%)	Median, 37.4	15 (15%)	63 (63%)	-0.54	11 (11%)
Control	69 (69%)	Median, 37.3	28 (28%)	74 (73%)	-0.35	12 (12%)
TE (95% CI)	OR, 0.51 (0.28 to 0.90)	NR	OR, 0.45 (0.22 to 0.89)	NR	-0.19% (-0.34% to -0.03%)	NR
p	.02	.50	.025	.18	.02	1.0

Values are n or n (%) or as otherwise indicated.
CGM: continuous glucose monitoring; CI: confidence interval; HbA1c: hemoglobin A_{1c}; NR: not reported; OR: odds ratio; RCT: randomized controlled trial; TE: treatment effect.

The purpose of the limitations tables (see Tables 7 and 8) is to display notable limitations identified in each study. This information is synthesized as a summary of the body of evidence following each table and provides the conclusions on the sufficiency of evidence supporting the position statement.

Table 7. Study Relevance Limitations of RCTs for Real-Time CGM in Pregnant People With Type 1 Diabetes

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Follow-Up[e]
Feig et al (2017)[22],	4. Run-in period requirement may have biased selection to highly compliant participants	3. More unscheduled contacts in CGM group	3. More unscheduled contacts in CGM group		

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
CGM: continuous glucose monitoring; RCT: randomized controlled trial.
[a] Population key: 1. Intended use population unclear; 2. Clinical context is unclear; 3. Study population is unclear; 4. Study population not representative of intended use; 5. Enrolled study populations do not reflect relevant diversity.
[b] Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4.Not the intervention of interest.
[c] Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively.
[d] Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. No CONSORT reporting of harms; 4. Not establish and validated measurements; 5. Clinical significant difference not prespecified; 6. Clinical significant difference not supported.
[e] Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms.

Table 8. Study Design and Conduct Limitations of RCTs for Real-Time CGM in Pregnant People With Type 1 Diabetes

Study	Allocation[a]	Blinding[b]	Selective Reporting[c]	Data Completeness[d]	Power[e]	Statistical[f]
Feig et al (2017)[22,]		1. Not blinded; chance of bias in clinical management				3, 4. Treatment effects and confidence intervals not calculated for some outcomes

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
CGM: continuous glucose monitoring; RCT: randomized controlled trial.
[a] Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias.
[b] Blinding key: 1. Not blinded to treatment assignment; 2. Not blinded outcome assessment; 3. Outcome assessed by treating physician.
[c] Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication.
[d] Data Completeness key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials).
[e] Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference.
[f] Statistical key: 1. Analysis is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event; 2. Analysis is not appropriate for multiple observations per patient; 3. Confidence intervals and/or p values not reported; 4.Comparative treatment effects not calculated.

Section Summary: Continuous Glucose Monitoring Devices for Long-Term Use in Type 1 Diabetes

Numerous RCTs and several systematic reviews of RCTs have evaluated CGM in patients with type 1 diabetes. RCTs have evaluated both real-time and intermittently scanned CGM devices. Two recent RCTs in patients who used multiple daily insulin injections and were highly compliant with CGM devices during run-in phases found that CGM was associated with a larger reduction in HbA1c levels than previous studies. Reductions were 0.4% and 0.6%, respectively, compared with approximately 0.2% to 0.3% in previous analyses. One of the 2 RCTs prespecified hypoglycemia-related outcomes and time spent in hypoglycemia were significantly lower in the CGM group.

One RCT in pregnant women with type 1 diabetes (n=215) has compared CGM with SMBG. Adherence was high in the CGM group. The difference in the change in HbA1c levels from baseline to 34 weeks of gestation was statistically significant favoring CGM, and women in the CGM group spent an increased percentage of time in the recommended glucose control target range at 34 weeks of gestation. There were no between-group differences in maternal hypoglycemia, gestational weight gain, or total daily insulin dose. A smaller proportion of infants of mothers in the CGM group were large for gestational age, had neonatal intensive care admissions lasting more than 24 hours, and had neonatal hypoglycemia requiring treatment. The total hospital length of stay was shorter by almost 1 day in the CGM group.

Continuous Glucose Monitoring Devices for Short-Term Use in Type 1 Diabetes

Clinical Context and Therapy Purpose

The purpose of the short-term use of CGM devices is to provide a testing option that is an alternative to or an improvement on existing testing used in the management of individuals with type 1 diabetes.

The question addressed in this evidence review is: Does the short-term use of a CGM device improve the net health outcome for individuals with type 1 diabetes?

The following PICO was used to select literature to inform this review.

Populations
The relevant population of interest is individuals with type 1 diabetes. All individuals with type 1 diabetes require engagement in a comprehensive self-management and clinical assessment program that includes assessment of blood glucose control. Individuals with type 1 diabetes may have poorly controlled diabetes, despite current use of best practices, including situations such as unexplained hypoglycemic episodes, hypoglycemic unawareness, suspected postprandial hyperglycemia, and recurrent diabetic ketoacidosis. In addition, individuals with type 1 diabetes may need to determine basal insulin levels prior to insulin pump initiation.

Interventions
The testing being considered is the short-term use of a CGM device to assess blood glucose levels as part of optimal diabetes management. Short-term use is generally for 72 hours. However, reports of use range from 3 to 30 days.

Comparators
The following practice is currently being used to measure glucose levels: capillary blood sampling (finger stick) for SMBG. Standard treatment for patients with type 1 diabetes includes injection of long-acting basal insulin plus MDI of rapid-acting insulin boluses as required for meal intake. Activity level may require patients need to modify the timing and dose of insulin administration. Individuals with type 1 diabetes may also use an insulin pump either for initial treatment or convert to pump use after a period of MDI. Individuals are required to check their blood glucose before making preprandial insulin calculations, in response to symptoms of hypoglycemia or related to activity-related insulin adjustments

Outcomes
For short-term use of CGM, the general outcomes of interest include time in range (generally glucose of 70 to 180 mg/dl), frequency and time spent in hypoglycemia, and frequency and time spent in hyperglycemia for the duration of the monitoring. Repeat CGM may be necessary to assess the impact of changes in management.

Study Selection
Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess long-term outcomes and adverse effects, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded.

Review of Evidence
Systematic Reviews
Meta-analyses of glucose monitoring devices for type 1 diabetes tend to combine studies of short-term glucose monitoring with studies of long-term CGM. For this body of evidence, there is variability in the definitions of short-term monitoring and the specific monitoring protocols used. Also, many of the trials of short-term monitoring have included additional interventions to optimize glucose control (e.g., education, lifestyle modifications).

Two meta-analyses were identified that reported separate subgroup analyses for short-term, intermittent monitoring. In a Cochrane review by Langendam et al (2012), 4 studies (n=216) compared real-time short-term glucose monitoring systems with SMBG, and the pooled effect estimate for change in HbA1c levels at 3 months was not statistically significant (MD change, -0.18; 95% CI, -0.42 to 0.05).[7,] The meta-analysis by Wojciechowski et al (2011), which assessed RCTs on CGM (described previously), also included a separate analysis of 8 RCTs of short-term intermittent

monitoring.[9,] On pooled analysis, there was a statistically significant reduction in HbA1c levels with short-term intermittent glucose monitoring compared with SMBG (WMD, -0.26; 95% CI, -0.45 to -0.06).

Randomized Controlled Trials

The largest RCT was the Management of Insulin-Treated Diabetes Mellitus (MITRE) trial, published by Newman et al (2009); it evaluated whether the use of the additional information provided by minimally invasive glucose monitors improved glucose control in patients with poorly controlled insulin-requiring diabetes.[23,] This 4-arm RCT was conducted at secondary care diabetes clinics in 4 hospitals in England. This trial enrolled 404 people over the age of 18 years, with insulin-treated diabetes (types 1 or 2) for at least 6 months, who were receiving 2 or more injections of insulin daily. Most (57%) participants had type 1 diabetes (41% had type 2 diabetes, 2% were classified as "other"). Participants had to have 2 HbA1c values of at least 7.5% in the 15 months before trial entry and were randomized to 1 of 4 groups. Two groups received minimally invasive glucose monitoring devices (GlucoWatch Biographer or MiniMed Continuous Glucose Monitoring System [CGMS]). Short-term glucose monitoring was used (i.e., monitoring was performed over several days at various points in the trial). These groups were compared with an attention control group (standard treatment with nurse feedback sessions at the same frequency as those in the device groups) and a standard control group (reflecting common practice in the clinical management of diabetes). Changes in HbA1c levels from baseline to 3, 6, 12, and 18 months were the primary indicator of short- to long-term efficacy. At 18 months, all groups demonstrated a decline in HbA1c levels from baseline. Mean percentage changes in HbA1c levels were -1.4% for the GlucoWatch group, -4.2% for the CGMS group, -5.1% for the attention control group, and -4.9% for the standard care control group. In the intention-to-treat analysis, no significant differences were found between any groups at any assessment times. There was no evidence that the additional information provided by the devices changed the number or nature of treatment recommendations offered by the nurses. Use and acceptability indicated a decline for both devices, which was most marked in the GlucoWatch group by 18 months (20% still using GlucoWatch vs 57% still using the CGMS). In this trial of unselected patients, glucose monitoring (CGMS on an intermittent basis) did not lead to improved clinical outcomes.

Pregnant People

Systematic Reviews

Voormolen et al (2013) published a systematic review of the literature on CGM during pregnancy.[24,] They identified 11 relevant studies (n=534). Two were RCTs, one of which was the largest of the studies (n=154). Seven studies used CGM devices that did not have data available in real-time; the remaining 4 studies used real-time CGM. Reviewers did not pool study findings; they concluded that the evidence was limited to the efficacy of CGM during pregnancy. The published RCTs are described next.

Randomized Controlled Trials

Three RCTs of short-term glucose monitoring in pregnant women with type 1 or type 2 diabetes are summarized in Tables 9 to 12 and the following paragraphs. While both trials included a mix of women with type 1 and type 2 diabetes, most women had type 1 diabetes in both trials, so the trials are reviewed in this section.

Voormolen et al (2018) reported results of the GlucoMOMS trial, a multicenter, open-label RCT conducted between 2011 and 2015 in the Netherlands including pregnant women age 18 years and over with either diabetes mellitus type 1 (n=109), type 2 (n=82), or gestational (n=109) diabetes requiring insulin therapy before 30 weeks of gestation. The trial compared blinded CGM (n=147) to standard treatment (n=153).[25,] Glycemic control was measured by CGM for 5 tp 7 days every 6 weeks in the CGM group and SMBC was used in both groups. The primary outcome was macrosomia (birth weight above the 90th percentile). The incidence of large-for-gestational-age was 31% in the CGM group and 28% in the standard treatment group (RR=1.1; 95% CI, 0.8 to 1.4). HbA1c levels were similar between treatment groups.

Secher et al (2013) randomized 154 women with type 1 (n=123) and type 2 (n=31) diabetes to real-time CGM in addition to routine pregnancy care (n=79) or routine pregnancy care alone (n=75).[26,] Patients in the CGM group were instructed to use the CGM device for 6 days before each of 5 study visits and were encouraged to use the devices continuously; 64% of participants used the devices per-protocol. Participants in both groups were instructed to perform 8 daily self-monitored plasma glucose measurements for 6 days before each visit. Baseline mean HbA1c levels were 6.6% in the CGM group and 6.8% in the routine care group. The 154 pregnancies resulted in 149 live births and 5 miscarriages. The prevalence of large-for-gestational-age infants (at least 90th percentile), the primary study outcome, was 45% in the CGM group and 34% in the routine care group. The difference between groups was not statistically significant (p=.19). Also, no statistically significant differences were found between groups for secondary outcomes, including the prevalence of preterm delivery and the prevalence of severe neonatal hypoglycemia. Women in this trial had low baseline HbA1c levels, which might explain the lack of impact of CGM on outcomes. Other factors potentially contributing to the negative findings included the intensive SMBG routine in both groups and the relatively low compliance rate in the CGM group.

Murphy et al (2008) in the U.K. randomized 71 pregnant women with type 1 (n=46) and type 2 (n=25) diabetes to CGM or usual care.[27,] The intervention consisted of up to 7 days of CGM at intervals of 4 to 6 weeks between 8 weeks and 32 weeks of gestation. Neither participants nor physicians had access to the measurements during sensor use; data were reviewed at study visits. In addition to CGM, the women were advised to measure blood glucose levels at least 7 times a day. Baseline HbA1c levels were 7.2% in the CGM group and 7.4% in the usual care group. The primary study outcome was maternal glycemic control during the second and third trimesters. Eighty percent of women in the CGM group wore the monitor at least once per trimester. Mean HbA1c levels were consistently lower in the intervention arm, but differences between groups were statistically significant only at week 36. For example, between 28 weeks and 32 weeks of gestation, mean HbA1c levels were 6.1% in the CGM group and 6.4% in the usual care group (p=.10). The prevalence of large-for-gestational-age infants (at least 90th percentile) was a secondary outcome. Thirteen (35%) of 37 infants in the CGM group were large-for-gestational age compared with 18 (60%) of 30 in the usual care group. The odds for reduced risk of a large-for-gestational-age infant with CGM was 0.36 (95% CI, 0.13 to 0.98; p=.05).

Table 9. RCT Characteristics for Short-Term CGM in Pregnant People With Type 1 Diabetes

Study; Registration	Countries	Sites	Dates	Participants	Interventions	
					Active	Comparator
Voormolen et al (2018)[25,]	Netherlands and Belgium	23	2011-2015	Pregnant women with type 1 (n=109) or type 2 (n=82) diabetes who were undergoing insulin therapy at gestational age <16 weeks, or women who were undergoing insulin treatment for gestational diabetes (n=109) at gestational age <30 weeks; mean age, 32 y; mean HbA1c, 52 mmol/mol.	CGM (for 5-7 days every 6 weeks) plus SOC (n=147)	SOC (n=153)
Secher et al (2013)[26,]; NCT00994357	Denmark	1	2009-2011	Pregnant women with type 1 (80%) or type 2 (20%) diabetes; mean gestational age, <14 wk); median HbA1c level, 6.7%; median age, 32 y	CGM (for 6 d before each study visit; encouraged to used continuously) plus SOC (n=79)	SOC (n=75)
Murphy et al (2008)[27,]; ISRCTN84461581	U.K.	2	2003-2006	Pregnant women with type 1 (65%) or type 2 (35%) diabetes; mean gestational age, 9.2 wk; mean HbA1c level, 7.3%; mean age, 31 y	CGM (up to 7 d of CGM at intervals of	SOC (n=33)

Study; Registration	Countries	Sites	Dates	Participants	Interventions
					4-6 wk) plus SOC (n=38)

CGM: continuous glucose monitoring; HbA1c: hemoglobin A_{1c}; NCT: national clinical trial; RCT: randomized controlled trial; SOC: standard of care.

Table 10. RCT Results for Short-Term CGM in Pregnant People With Type 1 Diabetes

Study	Infant				Maternal	
	Large-for-Gestational Age	Gestational Age at Delivery	Severe Hypoglycemia	Caesarean Section	HbA1c Levels at 36 Weeks of Gestation[a]	Severe Hypoglycemia
Voormolen et al (2018)[25,]						
N	290	290	290	290		NR
CGM	(31)	266	25 (18%)	23 (21%)		
Control	(28)	266	25 (17%)	26 (23%)		
TE (95% CI)	RR=1.1 (0.8 to 1.4)	1.1 (0.9 to 1.4)	1.0 (0.6 to 1.7)	NR	'No difference'	
p						
Secher et al (2013)[26,]						
N	154	154	145	154	NR	154
CGM	34 (45%)	Median, 263	9 (13%)	28 (37%)	Median, 6.0%	16%
Control	25 (34%)	Median, 264	10 (14%)	33 (45%)	Median, 6.1%	16%
TE (95% CI)	NR	NR	NR	NR	NR	NR
p	.19	.14	.88	.30	.63	.91
		Weeks				
Murphy et al (2008)[27,]						
N	71	71	68	69	71	NR
CGM	13 (35%)	Mean, 37.6	3 (8%)	27 (71%)	Mean, 5.8%	
Control	18 (60%)	Mean, 37.5	5 (17%)	21 (61%)	Mean, 6.4%	
TE (95% CI)	OR=0.36 (0.13 to 0.98)	NR	NR	NR	0.6% (CI NR)	
p	.05	.80	.50	.40	.007	

Values are n or n (%) or as otherwise indicated.
CGM: continuous glucose monitoring; CI: confidence interval; HbA1c: hemoglobin A_{1c}; NR: not reported; OR: odds ratio; RCT: randomized controlled trial; TE: treatment effect.
[a] N inconsistently reported for HbA1c outcome.

Tables 11 and 12 display notable limitations identified in each study.

Table 11. Study Relevance Limitations of RCTs of Intermittent CGM in Pregnant People With Type 1 Diabetes

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Follow-Up[e]
Voormolen et al (2018)[25,]		4. Only 66% of the participants used devices per protocol			
Secher et al (2013)[26,]	4. Study population had relatively low HbA1c levels	4. Only 64% of the participants used devices per protocol			
Murphy et al (2008)[27,]					

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
CGM: continuous glucose monitoring; HbA1c: hemoglobin A_{1c}; RCT: randomized controlled trial.
[a] Population key: 1. Intended use population unclear; 2. Clinical context is unclear; 3. Study population is unclear; 4. Study population not representative of intended use; 5. Enrolled study populations do not reflect relevant diversity.
[b] Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator;

4.Not the intervention of interest.
[c] Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively.
[d] Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. No CONSORT reporting of harms; 4. Not establish and validated measurements; 5. Clinical significant difference not prespecified; 6. Clinical significant difference not supported.
[e] Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms.

Table 12. Study Design and Conduct Limitations of RCTs of Short-Term CGM Glucose Monitoring in Pregnant People With Type 1 Diabetes

Study	Allocation[a]	Blinding[b]	Selective Reporting[c]	Data Completeness[d]	Power[e]	Statistical[f]
Voormolen et al (2018)[25,]		1. Not blinded; chance of bias in clinical management				
Secher et al (2013)[26,]		1. Not blinded; chance of bias in clinical management				3, 4. Treatment effects and confidence intervals not calculated
Murphy et al (2008)[27,]		1. Not blinded; chance of bias in clinical management				3, 4. Treatment effects and confidence intervals not calculated for some outcomes

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
CGM: continuous glucose monitoring; RCT: randomized controlled trial.
[a] Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias.
[b] Blinding key: 1. Not blinded to treatment assignment; 2. Not blinded outcome assessment; 3. Outcome assessed by treating physician.
[c] Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication.
[d] Data Completeness key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials).
[e] Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference.
[f] Statistical key: 1. Analysis is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event; 2. Analysis is not appropriate for multiple observations per patient; 3. Confidence intervals and/or p values not reported; 4.Comparative treatment effects not calculated.

Section Summary: Glucose Monitoring Devices for Short-Term Use in Type 1 Diabetes

For short-term monitoring of type 1 diabetes, there are few RCTs and systematic reviews. The evidence for short-term monitoring on glycemic control is mixed, and there was no consistency in HbA1c levels. Some trials have reported improvements in glucose control for the intermittent monitoring group but limitations in this body of evidence preclude conclusions. The definitions of control with short-term CGM use, duration of use and the specific monitoring protocols varied. In some studies, short-term monitoring was part of a larger strategy aimed at optimizing glucose control, and the impact of monitoring cannot be separated from the impact of other interventions. Studies have not shown an advantage for intermittent glucose monitoring in reducing severe hypoglycemia events but the number of events reported is generally small and effect estimates are imprecise. The limited duration of use may preclude an assessment of any therapeutic effect. RCTs of

short-term CGM use for monitoring in pregnancy included women with both type 1 and 2 diabetes, with most having type 1 diabetes. One trial reported a difference in HbA1c levels at 36 weeks; the proportion of infants that were large for gestational age (>90th percentile) favored CGM while other trials did not. The differences in the proportions of infants born via cesarean section, gestational age at delivery, and infants with severe hypoglycemia were not statistically significant.

Continuous Glucose Monitoring Devices for Use in Individuals with Type 2 Diabetes Who Are Treated with Insulin Therapy

There is limited ability to distinguish between long-term and short-term glucose monitoring in the analysis of the data for type 2 diabetes, consistent with the literature.

Clinical Context and Therapy Purpose

The purpose of long-term and short-term CGM devices is to provide a treatment option that is an alternative to or an improvement on existing therapies such as SBGM.

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is individuals with type 2 diabetes who are treated with insulin therapy and who experience poor diabetes control despite current use of best practices. Poor control includes situations such as unexplained hypoglycemic episodes, hypoglycemic unawareness, and persistent hyperglycemia and A1C levels above target.

In addition, some individuals with type 2 diabetes may need to determine basal insulin levels prior to insulin pump initiation.

All individuals with type 2 diabetes require engagement in a comprehensive self-management and clinical assessment program that includes assessment of blood glucose control.

Interventions

The testing being considered is the use of long-term or short-term CGM devices to assess blood glucose levels as part of optimal diabetes management.

Comparators

Blood glucose monitoring is an essential component of type 2 diabetes management in order to monitor for and prevent hypoglycemia and hyperglycemia. For these individuals, guidelines recommend blood glucose monitoring prior to meals and snacks, at bedtime, occasionally postprandially, prior to exercise, when low blood glucose is suspected, after treating low blood glucose, and prior to and while performing critical tasks such as driving. The following practice is currently being used to measure glucose levels: SMBG (capillary blood sampling (finger stick) using blood glucose meters) and periodic measurement of HbA1c.

Outcomes

The general outcomes of interest are change in HbA1c levels, frequency of and time spent in hypoglycemia, frequency and time spent in hyperglycemia, complications of hypoglycemia and hyperglycemia, and QOL. To assess short-term outcomes such as HbA1c levels, a minimum follow-up of 8 to 12 weeks is appropriate. To assess long-term outcomes such as time spent in hypoglycemia, the incidence of hypoglycemic events, complications of hypoglycemia, and QOL, follow-up of 6 months to 1 year would be appropriate.

Study Selection

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;

- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess long-term outcomes and adverse effects, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded.

Review of Evidence

Randomized Controlled Trials

Three RCTs evaluated CGM in individuals with type 2 diabetes using multiple daily insulin injections or an insulin pump (Tables 13 and 14).[28,29,30,] One evaluated real-time CGM using the Dexcom device and 2 evaluated intermittently scanned CGM using the Freestyle Libre system.

Beck et al (2017) reported on the DIAMOND RCT.[28,] DIAMOND compared CGM with the Dexcom device to SMBG in 158 participants at 25 endocrinology practices in North America (22 in the U.S., 3 in Canada). Participants who were adherent during a run-in period were eligible for randomization. Change in HbA1c level from baseline to 24 weeks was the primary outcome. Analyses were adjusted for baseline HbA1c levels and were performed using intention-to-treat analysis with missing data handling by multiple imputations. Week 24 follow-up was completed by 97% of the CGM group and 95% of the control group. Mean CGM use was greater than 6 days/week at 1 month, 3 months, and 6 months. The adjusted difference in mean change in HbA1c level from baseline to 24 weeks was -0.3% (95% CI, -0.5% to 0.0%; p=.022) favoring CGM. The adjusted difference in the proportion of patients with a relative reduction in HbA1c level of 10% or more was 22% (95% CI, 0% to 42%; p=.028) favoring CGM. There were no events of severe hypoglycemia or diabetic ketoacidosis in either group. The treatment groups did not differ in any of the QOL measures.

Haak et al (2017) compared intermittently scanned CGM with the Freestyle Libre device in 224 individuals at 26 European centers. [29,] At 6 months, there was no difference between groups in the primary outcome of change in HbA1c (p=.8222). However, results for secondary outcomes including time in hypoglycemia and treatment satisfaction favored the CGM group. No serious adverse events or severe hypoglycemic events were reported related to device use.

Yaron et al (2019) reported higher treatment satisfaction (the primary outcome) in 101 individuals using a flash glucose monitor compared to SMBG.[30,] On secondary glycemic control measures, HbA1c was reduced by 0.82% compared to 0.33% in the control group (p=.005) without an increase in the frequency of hypoglycemic events.

One RCT evaluated CGM in patients treated with basal insulin. Martens et al (2021) reported results of an RCT comparing real-time CGM with SMBG in 176 patients with poorly controlled type 2 diabetes (HbA1c levels 7.8% to 11.5%) treated with basal insulin without prandial insulin.[31,] At 8 months, there was a statistically significantly greater decrease in mean HbA1c in the CGM group (adjusted difference, -0.4%; 95% CI -0.8% to -0.1%; p=.02), with 1 hypoglycemic event in each group. Aleppo et al (2021) reported a 6-month follow-up study of 163 patients who had been randomized in this same trial (93.1%).[32,] Patients originally randomized to SMBG continued to use SMBG for another 6 months, and the CGM group was randomly reassigned either to continue CGM or discontinue CGM and resume SMBG. In the group that discontinued CGM, mean HbA1c increased from 7.9% at 8 months to 8.2% at 14 months, whereas in the group that continued CGM, mean HbA1c decreased from 8.2% to 8.1%.

Table 13. Key RCT Characteristics for CGM in Individuals with Type 2 Diabetes on Insulin

Study; Registration	Countries	Sites	Dates	Participants	Interventions	
					Active	Comparator
Beck et al (2017) (DIAMOND)[28,];	U.S., Canada	25	2014-2016	Adults with T2D using multiple daily injections of insulin with	Real-time CGM (n=79)	SMBG (n=79)

Study; Registration	Countries	Sites	Dates	Participants	Interventions	
NCT02282397				HbA1c levels 7.5%-10.0% (baseline mean, 8.5%); mean age, 60 y		
Haak et al (2017)[29,] NCT02082184	Multiple European	26	2014-2015	Adults with T2D treated with insulin for at least 6 months and on their current regimen for 3 months or more; HbA1c 7.5 to 12.0%	Flash glucose monitoring with FreeStyle Libre device n=149	SMBG n=75
Yaron et al (2019)[30,] NCT02809365	Israel	2	2016-2017	Adults with T2D on multiple daily insulin injections for at least 1 year	Flash glucose monitoring with FreeStyle Libre device n=53	SMBG n=48
Martens et al (2021)[31,]Aleppo et al (2021)[32,]	U.S.	15	2018-2019	Adults with T2D treated with 1 to 2 daily injections of basal insulin without prandial insulin; HbA1c levels 7.8% to 11.5% (baseline mean, 9.1%); mean age, 57 y	Real-time CGM (n=116)	SMBG (n=59)

CGM: continuous glucose monitoring; HbA1c: hemoglobin A_{1c}; NCT: national clinical trial;NR: not reported; RCT: randomized controlled trial; SMBG: self-monitored blood glucose; T2D: type 2 diabetes.

Table 14. Key RCT Outcomes for CGM in Individuals with Type 2 Diabetes on Insulin

Study	Reduction in HbA1c Levels (Mean Range), %	HbA1c Level <7.0%, n (%)	Relative Reduction in HbA1c Level ≥10%, n (%)	Hypoglycemic or Ketoacidosis Events	Diabetes Complications (retinopathy, nephropathy, neuropathy, diabetic foot)	Health-Related Quality of Life
	Baseline to 24 Wk	At 24 Wk	At 24 Wk			DTSQ Overall Mean Score at 24 Wk
Beck et al (2017)[28,]						
N	158	158	158	158	NR	150
CGM	8.6 to 7.7	11 (14%)	40 (52%)	0		Baseline: 1.78 24 weeks: 1.61
Control	8.6 to 8.2	9 (12%)	24 (32%)	0		Baseline: 1.69 24 weeks: 1.78
TE (95% CI)	-0.3 (-0.5 to 0.0)	3% (-9% to 14%)	22% (0% to 42%)			0.22 (0.08 to 0.36)
p	.022	.88	.028			.009
Haak et al (2017)[29,] NCT02082184	HbA1c change from baseline to 6 months: -3.1 (SE 0.75) mmol/L (-			Time in hypoglycemia: <3.9 mmol/L: reduced by mean 0.47 (SE		

Study	Reduction in HbA1c Levels (Mean Range), %	HbA1c Level <7.0%, n (%)	Relative Reduction in HbA1c Level ≥10%, n (%)	Hypoglycemic or Ketoacidosis Events	Diabetes Complications (retinopathy, nephropathy, neuropathy, diabetic foot)	Health-Related Quality of Life
	0.29% ± 0.07%) vs. -3.4 (SE 1.04 [-0.31 ± 0.09%]) p=.8222			0.13) hours/day; p=.0006 <3.1 mmol/L reduced by 0.22 ± 0.07 hours/day; p=.0014		
Yaron et al (2019)[30,]	Change in HbA1c −0.82% (9 mmol/mol) vs. −0.33% (3.6 mmol/mol) p=.005				NR	Treatment satisfaction (Primary outcome, DTSQc) at 10 weeks: 2.47 (0.77) vs. 2.18 (0.83); p=.053
Martens et al (2021)[31,]Aleppo et al (2021)[32,]NCT03566693						
N	156	156	156	175	NR	NR
CGM	9.1 to 8.0	20 (19%)	66 (63%)	1 hyopglycemic event, 1 ketoacidosis event		
Control	9.0 to 8.4	5 (10%)	21 (41%)	1 hypoglycemic event		
TE (95% CI)	-0.4 (-0.8 to -0.1)	11.8 (0.6 to 24.5)	22.4 (12.0 to 32.0)			
p	.02	.04	<.001			

CGM: continuous glucose monitoring; CI: confidence interval; DTSQ: Diabetes Treatment Satisfaction; HbA1c: hemoglobin A_{1c}; NCT: national clinical trial; NR: not reported; RCT: randomized controlled trial; SE: standard error; TE: treatment effect.
[a] serious hypoglycemic event defined as requiring third-party assistance.

Observational Studies

Because several RCTs exist, observational studies will be summarized briefly below only if they capture longer periods of follow-up (>6 months), larger populations, or particular subgroups of interest.

Long-term follow-up

Observational studies with follow-up of more than 6 months including adults with type 2 diabetes, the majority of whom were on insulin, have shown that reduction in mean HbA1c is maintained for 12 months,[33,] and reductions in acute diabetes events, including severe hypoglycemia and diabetic ketoacidosis are maintained for 1 to 2 years.[20,34,21,]

Individuals with Significant Hypoglycemia

Twelve-month open-access, follow-up results for long-term CGM with the Freestyle Libre device in 108 individuals from the Haak et al (2017) 6-month trial were reported in a second publication by Haak et al (2017).[35,] Hypoglycemia was analyzed using 3 different glucose level thresholds (<70 mg/dl, <55 mg/dl, and <45 mg/dl). At 12-month follow-up, hypoglycemic events were reduced by 40.8% to 61.7% with a greater relative reduction in the most severe thresholds of hypoglycemia. At all 3 glucose level thresholds, there were statistically significant reductions in time in hypoglycemia, frequency of hypoglycemic events, time in nocturnal hypoglycemia, and frequency of nocturnal hypoglycemia. Change for hypoglycemic events per day at 12 months compared to baseline was also significant: -40.8% (glucose <70 mg/dl; p<.0001); -56.5% (glucose <55 mg/dl; p<.0001); -61.7% (glucose <45 mg/dl; p=.0001).

Pregnant People

Wilkie et al (2023) reported results of a systematic review of CGM in type 2 diabetes in pregnancy.[36,] The review includes the same 3 RCTs described below. The meta-analytic treatment effect estimate of large-for-gestational-age infants (CGM, n=56 vs. control, n=53) was OR, 0.8 (95% CI, 0.3 to 1.8). There was no difference in development of preeclampsia (OR, 1.6, 95% CI, 0.3 to 7.2).

As discussed in the section on CGM in pregnant women with type 1 diabetes, 3 RCTs have evaluated short-term glucose monitoring in pregnant women with type 1 and type 2 diabetes. Most women had type 1 diabetes in both trials. There were 25 (35%) women with type 2 diabetes in Murphy et al (2008)[27,] and 31 (20%) with type 2 diabetes in Secher et al (2013)[26,]and 82 (27%) women with type 2 diabetes in Voormolen (2018).[25,] Results for women with type 2 diabetes were not reported in Murphy et al (2008). Secher et al (2013) reported that 5 (17%) women with type 2 diabetes experienced 15 severe hypoglycemic events, with no difference between groups; other analyses were not stratified by diabetes type.

Section Summary: Continuous Glucose Monitoring Devices for Use in Individuals with Type 2 Diabetes Who Are Treated with Insulin

Three RCTs have evaluated CGM compared to SMBG in individuals with type 2 diabetes on intensive insulin therapy, 1 using real-time CGM and 2 using an intermittently scanned device. One RCT evaluated CGM in patients treated with basal insulin using real-time CGM. All found either improved glycemic outcomes or no difference between groups with no increase in hypoglycemic events. In the DIAMOND trial, the adjusted difference in mean change in HbA1c level from baseline to 24 weeks was -0.3% (95% CI, -0.5% to 0.0%; p=.022) favoring CGM. The adjusted difference in the proportion of patients with a relative reduction in HbA1c level of 10% or more was 22% (95% CI, 0% to 42%; p=.028) favoring CGM. There were no events of severe hypoglycemia or diabetic ketoacidosis in either group. Yaron et al (2019) reported higher treatment satisfaction with CGM compared to control (the primary outcome). At 12-month follow-up in one of the trials of the Freestyle Libre device, hypoglycemic events were reduced by 40.8% to 61.7% with a greater relative reduction in the most severe thresholds of hypoglycemia. In the Martens trial of individuals treated with basal insulin without prandial insulin, there was a statistically significantly greater decrease in mean HbA1c in the CGM group (adjusted difference, -0.4%; 95% CI -0.8% to -0.1%; p=.02), with 1 hypoglycemic event in each group.

Continuous Glucose Monitoring Devices for Use in Individuals with Type 2 Diabetes Who Are Not Treated with Insulin Therapy

Clinical Context and Therapy Purpose

The purpose of long-term and short-term CGM devices is to provide a treatment option that is an alternative to or an improvement on existing therapies in individuals with type 2 diabetes.

The question addressed in this evidence review is: Does the use of long-term or short-term CGM devices improve the net health outcome for individuals with type 2 diabetes on less intensive therapy (i.e., who do not require multiple daily insulin injections or an insulin pump)?

The following PICO was used to select literature to inform this review.

Populations
The relevant population of interest is individuals with type 2 diabetes who are not treated with insulin therapy.

All individuals with type 2 diabetes require engagement in a comprehensive self-management and clinical assessment program that includes assessment of blood glucose control.

Interventions
The testing being considered is the long-term or short-term use of CGM devices to assess blood glucose levels as part of optimal diabetes management.

Currently, CGM devices are of 2 designs; rtCGM provides real-time data on glucose level, glucose trends, direction, and rate of change, and iCGM devices that show continuous glucose measurements retrospectively. These devices are also known as flash-glucose monitors.

Comparators
SMBG (capillary blood sampling [finger stick]) using blood glucose meters and periodic measurement of HbA1c is used to measure glucose levels.

In contrast to recommendations in individuals on intensive insulin regimens, guidelines are less clear on when to prescribe blood glucose monitoring and how often monitoring is needed in individuals with type 2 diabetes who are not on insulin therapy. In individuals on oral antidiabetic agents only, routine glucose monitoring may be of limited additional clinical benefit.[37,]

Outcomes
The general outcomes of interest are change in HbA1c levels, frequency of and time spent in hypoglycemia, frequency and time spent in hyperglycemia, complications of hypoglycemia and hyperglycemia, and QOL. To assess short-term outcomes such as HbA1c levels, a minimum follow-up of 8 to 12 weeks is appropriate. To assess long-term outcomes such as time spent in hypoglycemia, the incidence of hypoglycemic events, complications of hypoglycemia, and QOL, follow-up of 6 months to 1 year would be appropriate.

Study Selection
Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess long-term outcomes and adverse effects, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded.

There is limited ability to distinguish between long-term and short-term glucose monitoring in the analysis of the data for type 2 diabetes, consistent with reporting in the literature. Therefore, this section includes both long-term and short-term uses.

Review of Evidence
Randomized Controlled Trials
Four RCTs evaluated CGM in individuals with Type 2 diabetes who are not treated with insulin therapy (Tables 15 and 16).

Ehrhardt et al (2011) reported the results of a RCT evaluating the intermittent use of a CGM device over 12 weeks in adults with type 2 diabetes treated with diet/exercise and/or glycemia-lowering medications but not prandial insulin who had an initial HbA1c level of at least 7% but not more than 12%.[38,] Twenty-nine of 100 participants (29.0%) were using basal insulin alone or in combination with oral agents. The trial compared real-time CGM with the Dexcom device used for 4 cycles (2 weeks on and 1 week off) with SMBG. Vigersky et al (2012) reported follow up data through 52 weeks.[39,] The primary efficacy outcome was a mean change in HbA1c levels. Mean HbA1c levels in the CGM group were 8.4% at baseline, 7.4% at 12 weeks, 7.3% at 24 weeks, and 7.7% at 52 weeks. In the SMBG group, these values were 8.2% at baseline, 7.7% at 12 weeks, 7.6% at 24 weeks, and 7.9% at 52 weeks. During the trial, the reduction in HbA1c levels was significantly greater in the CGM group than in the SMBG group (p=.04). After adjusting for potential confounders (e.g., age, sex, baseline therapy, whether the individual started taking insulin during the study), the difference between groups over time remained statistically significant (p<.001). The investigators also evaluated SMBG results for both groups. The mean proportions of SMBG tests less than 70 mg/dL were 3.6% in the CGM group and 2.5% in the SMBG group (p=.06).

Price et al (2021) reported results from the COntinuous Glucose Monitoring & Management In TypE 2 Diabetes (COMMITED; NCT03620357) RCT comparing rt-CGM (10 days a month for 3 months) to SMBG in adult patients with type 2 diabetes (HbA1c between 7.8% and 10.5%) who were receiving 2 or more oral antidiabetic drugs, but not insulin, in the U.S. and Canada between 2018 and 2020.[40,] Participants were 47% female, 74% White, 14% Asian, 7% Black and 29% Hispanic. The mean age was 60 years. The change in HbA1c at week 12 was not statistically different (-0.5 (1.3)% vs -0.2 (1.1)% for the CGM and SMBG groups, respectively; p=.74). The reduction in HbA1c was not sustained at month 9 for either group (-0.2 (0.9)% vs 0.1 (1.3)%, respectively, for CGM versus SMBG groups (p=.79).

Wada et al (2020) reported results of an open-label, multicenter RCT in Japan including participants with non-insulin-treated type 2 diabetes with HbA1c ≥7.5% and <8.5%.[41,] The trial compared flash glucose monitoring worn for 12 weeks (n=49) and conventional SMBG (n=51). The primary outcome was change in HbA1c level at 12 weeks. There was no significant between-group difference in the change from baseline in the 2 groups at 12 weeks (CMG, -0.43% vs. SMBG, -0.30%; difference=-0.13%; 95% CI, −0.35 to 0.09; p=.24) but there was a difference favoring CGM at 24 weeks (difference, −0.29%; 95% CI, −0.54 to −0.05; p=.02).

Aronson et al (2022) reported results of the IMMEDIATE multicenter RCT (NCT04562714) conducted in Canada including adults with type 2 diabetes and HbA1c of 7.5% or higher who were using at least 1 non-insulin antihyperglycemic therapy.[42,] The 2 treatment groups were the flash glucose monitor CGM group (FreeStyle Libre Pro; n=58) worn 14 days at baseline and again at week 14 plus diabetes self-management education versus diabetes self-management education alone (DSME; n=58). DSME included instruction to self-monitor blood glucose at least 4 times daily. The primary outcome was the difference in percentage mean Time In Range (TIR; glucose 70-180 mg/dl) at 16 weeks. At 16 weeks, the CGM group had significantly greater mean TIR (difference=9.9%; 2.4 hours; 95% CI, 17.3% to 2.5%; p<.01).The mean HbA1c at 16 weeks was 7.6% in the CGM group compared to 8.1% in the DSME group (adjusted mean difference, 0.3%; 95% CI, 0% to 0.7%; p=.05). The Glucose monitoring satisfaction score was higher in the CGM group compared with the DSME group but there were no differences in the other patient-reported outcomes (Diabetes Distress Score, Adherence to Refills and Medications Scale for Diabetes and Skills, Confidence & Preparedness Index).

Tables 17 and 18 display notable limitations identified in the studies. These include a lack of blinding and heterogeneity in the participant populations, lack of data on diabetic events and percent of patients meeting target goals, and insufficient duration to determine effects on diabetic complications.

Table 15. Key RCT Characteristics for CGM in Individuals with Type 2 Diabetes not on Insulin Therapy

Study; Registration	Countries	Sites	Dates	Participants	Interventions	
					Active	Comparator
Ehrhardt et al (2011)[38],Vigersky et al (2012) [39],	U.S.	1	NR	Adults with T2D using oral antidiabetic agents without prandial insulin; HbA1c levels 7.0% to 12.0% (baseline mean, 8.3%); mean age, 58 y 29 of 100 (29%) were using basal insulin	Real-time CGM for 4 cycles of 3 wk (n=50)	SMBG (n=50)
Price et al (2021)[40],	U.S. and Canada	8	2018-2020	Adults with T2D receiving 2+ oral antidiabetic drugs, HbA1c between 7.8% and 10.5%, not receiving insulin; mean age, 60 y, mean HbA1c, 8.4%	Real-time CGM (Dexcom G6) for 10 days a month for 3 months (n=46)	SMBG (n=24)
Wada et al (2020)[41],	Japan	5	2017-2018	Ages 20 to 70 with non-insulin-treated type 2 diabetes with HbA1c ≥7.5%and <8.5%; mean age, 58 y; mean HbA1c, 7.8%	Flash glucose monitor (Freestyle Libre) for 12 weeks (n=49)	SMBG schedule not described (n=51)
Aronson (2022)[42],	Canada	6	2020-2021	Adults with type 2 diabetes and HbA1c ≥7.5% who were using at least one non-insulin antihyperglycemic therapy; mean age, 58y; mean HbA1c, 8.6%	Flash glucose monitor (FreeStyle Libre Pro) for 14 days plus diabetes self-management education (n=58)	Diabetes self-management education alone (included SMBG) (n=58)

CGM: continuous glucose monitoring; HbA1c: hemoglobin A_{1c}; ; NR: not reported; RCT: randomized controlled trial; SMBG: self-monitored blood glucose; T2D: type 2 diabetes.

Table 16. Key RCT Outcomes for CGM in Individuals with Type 2 Diabetes not on Insulin Therapy

Study	HbA1c Levels (Mean Range), %	HbA1c Level <7.0%, n (%)	Relative Reduction in HbA1c Level ≥10%, n (%)	Hypoglycemic or Ketoacidosis Events	Diabetes Complications (retinopathy, nephropathy, neuropathy, diabetic foot)	Patient Reported Outcomes
Ehrhardt et al (2011)[38], Vigersky et al (2012) [39],						
N	100	NR	NR	NR	NR	NR
CGM	8.4 to 7.4					
Control	8.2 to 7.7					
TE (95% CI)	NR					
p	.006					
Price et al (2021)[40],	At week 12	At week 12	NR			
N	67	67				
CGM	8.0 (1.1)	(18%)		0		
Control	8.1 (1.0)	(9%)		1		

Study	HbA1c Levels (Mean Range), %	HbA1c Level <7.0%, n (%)	Relative Reduction in HbA1c Level ≥10%, n (%)	Hypoglycemic or Ketoacidosis Events	Diabetes Complications (retinopathy, nephropathy, neuropathy, diabetic foot)	Patient Reported Outcomes
TE (95% CI)	NR			NR		
p	.74	.26		NR		
Wada et al (2020)[41,]	Change from baseline to 12 weeks	NR	NR	Hypoglycemia, n		Diabetes Treatment Satisfaction Questionnaire (DTSQ) score, mean (SD)
N	93			93		90
CGM	-0.43			2		35 (5)
Control	-0.30			1		31 (7)
TE (95% CI)	-0.13 (-0.35 to 0.09)			NR		NR
p	.24			NR		<.001
Aronson (2022)[42,]	At 16 weeks	NR	NR	At least one hypoglycemic event, n(%)	NR	Glucose monitoring satisfaction score (GMSS), mean (SD) at week 16
N	108					NR
CGM	7.6			30 (59%)		3.9 (0.5)
Control	8.1			24 (50%)		3.4 (0.5)
TE (95% CI)	0.3% (0.0 to 0.7) favoring CGM			NR		0.5 (0.7 to 0.3) favoring CGM
p	.05			NR		<.01

CGM: continuous glucose monitoring; CI: confidence interval; DDS: Diabetes Distress Scale; DTSQ: Diabetes Treatment Satisfaction; HbA1c: hemoglobin A_{1c}; NCT: national clinical trial;NR: not reported; RCT: randomized controlled trial; TE: treatment effect.
[a] serious hypoglycemic event defined as requiring third-party assistance.

Table 17. Study Relevance Limitations of RCTs of CGM in Individuals with Type 2 Diabetes Not on Insulin Therapy for Glucose Monitoring in Type 2 Diabetes

Study; Trial	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Follow-Up[e]
Ehrhardt et al (2011)[38,] Vigersky et al (2012) [39,]	1. study population a mix of participants using basal insulin or oral agents alone			1. Focused on HbA1c; did not include outcomes on adverse events, QOL, or diabetic complications 6. No justification for clinically significant difference	1. Follow-up not sufficient to determine effects on diabetic complications
Price et al (2021)[40,]					1. Treatment and follow-up of 3 months
Wada et al (2020)[41,]	5. Study conducted in Japan			1. Did not report key outcomes on participants meeting target A1c levels	1. Treatment for 12 weeks with 12 additional weeks of follow-up
Aronson (2022)[42,]	5. Study conducted in Canada			1. Did not report key outcomes on participants meeting target A1c levels	1. Follow-up of 16 weeks

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.

CGM: continuous glucose monitoring; HbA1c: hemoglobin A_{1c}; QOL: quality of life; RCT: randomized controlled trial.
[a] Population key: 1. Intended use population unclear; 2. Clinical context is unclear; 3. Study population is unclear; 4. Study population not representative of intended use; 5. Enrolled study populations do not reflect relevant diversity.
[b] Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4.Not the intervention of interest.
[c] Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively.
[d] Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. No CONSORT reporting of harms; 4. Not establish and validated measurements; 5. Clinical significant difference not prespecified; 6. Clinical significant difference not supported.
[e] Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms.

Table 18. Study Design and Conduct Limitations of RCTs of CGM in Individuals with Type 2 Diabetes Not on Insulin Therapy

Study; Trial	Allocation[a]	Blinding[b]	Selective Reporting[c]	Data Completeness[d]	Power[e]	Statistical[f]
Ehrhardt et al (2011)[38], Vigersky et al (2012) [39],		1. Not blinded; chance of bias in clinical management				
Price et al (2021)[40],		1. Not blinded			1, 2, 3: No information on power or sample size calculations	
Wada et al (2020)[41],		1. Not blinded				
Aronson (2022)[42],		1. Not blinded				

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
CGM: continuous glucose monitoring; RCT: randomized controlled trial.
[a] Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias.
[b] Blinding key: 1. Not blinded to treatment assignment; 2. Not blinded outcome assessment; 3. Outcome assessed by treating physician.
[c] Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication.
[d] Data Completeness key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials).
[e] Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference.
[f] Statistical key: 1. Analysis is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event; 2. Analysis is not appropriate for multiple observations per patient; 3. Confidence intervals and/or p values not reported; 4.Comparative treatment effects not calculated.

Section Summary: Continuous Glucose Monitoring Devices for Use in Individuals with Type 2 Diabetes Who Are Not Treated with Insulin Therapy

The trials reported mixed results with respect to benefits of CGM regarding glycemic control. However, participant populations were heterogenous with regard to their diabetic treatment regimens, and participants might not have been receiving optimal therapy. In individuals on oral antidiabetic agents only, routine glucose monitoring may be of limited additional clinical benefit. Additional evidence would be needed to show what levels of improvements in HbA1c over the short-term in this population would be linked to meaningful improvements over the long-term in health outcomes such as diabetes-related morbidity and complications.

Continuous Glucose Monitoring Use in Pregnant People With Gestational Diabetes

Clinical Context and Therapy Purpose

The purpose of long-term CGM and short-term (intermittent) glucose monitoring devices is to provide a treatment option that is an alternative to or an improvement on existing therapies in persons with gestational diabetes.

The question addressed in this evidence review is: Do the use of long-term CGM and short-term (intermittent) glucose monitoring devices improve the net health outcome for women with gestational diabetes?

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest are persons with gestational diabetes.

Interventions

The testing being considered are devices that provide continuous, long-term glucose levels to the patient to direct insulin regimens and intermittent (i.e., 72 hours), short-term monitoring of glucose levels used by the provider to optimize management.

Comparators

The following practice is currently being used to measure glucose levels: capillary blood sampling (finger stick) for blood glucose meters for self-monitoring.

Outcomes

The general outcomes of interest are a change in HbA1c levels, time spent in hypoglycemia, the incidence of hypoglycemic events, complications of hypoglycemia, and QOL.

To assess short-term outcomes such as HbA1c levels, time spent in hypoglycemia, the incidence of hypoglycemic events, and complications of hypoglycemia, a minimum follow-up of 8 to 12 weeks is appropriate. To assess long-term outcomes such as QOL and maternal and infant outcomes, follow-up of 24 to 36 weeks would be appropriate.

Study Selection

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess long-term outcomes and adverse effects, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded.

Review of Evidence

Randomized Controlled Trials

Two trials of glucose monitoring in women with gestational diabetes have been published. Trial characteristics, results, and limitations for the RCTs limited to gestational diabetes are shown in Tables 19 to 22 and briefly described below. In addition, the GlucoMOMS trial described in the previous section on pregnant women with type 1 diabetes also included 109 women with gestational diabetes.[25,]

Lai et al (2023) published results of an RCT comparing CGM plus SMGB (n=77) to SMGB (n=77) in pregnant people with gestational diabetes at 24 to 28 gestation with HbA1c <6% between 2019 and

2021 at a single center in China (NCT03955107).[43,] Study visits occurred at 4 and 8 weeks. Participants in the CGM group were provided with a Medtronic CGM system that measured subcutaneous interstitial glucose for 3 consecutive days and were instructed to use CGM every 4 weeks (0, 4, and 8 weeks). The SMBG group was instructed to perform SMBG 4 times per day for 3 consecutive days every 4 weeks (0, 4 and 8 weeks). Participants in both groups continued their usual protocol of capillary glucose monitoring during their pregnancy and were asked to perform SMBG at least 7 times weekly. Most outcomes did not differ by treatment group with the exception of proportion of participants within recommended gestational weight gain (59.7% vs. 40.3%, p=.046).

In the RCT, Wei et al (2016) evaluated the use of CGM in 120 women with gestational diabetes at 24 to 28 weeks.[44,] Patients were randomized to prenatal care plus CGM (n=58) or SMBG (n=62). The CGM sensors were reportedly inserted for 48 to 72 hours on weekdays; it is not clear whether the readings were available in real-time. The investigators assessed a number of endpoints and did not specify primary outcomes; a significance level of p<.05 was used for all outcomes. The groups did not differ significantly in a change in most outcomes, including a change in maternal HbA1c levels, rates of preterm delivery before the 35th gestational week, cesarean delivery rates, proportions of large-for-gestational-age infants, or rates of neonatal hypoglycemia. Women in the CGM group gained significantly less weight than those in the SMBG group.

Table 19. Key RCT Characteristics for CGM in Pregnant People With Gestational Diabetes

Study	Countries	Sites	Dates	Participants	Interventions	
					Active	Comparator
Lai et al (2023)[43,]	China	1	2019-2021	Pregnant people with gestational diabetes with HbA1c <6% at 24–28 gestational weeks; singleton pregnancy, preconception BMI ≥18 kg/m2; mean HbA1c level, 5.9%; mean age, 32 y	CGM + SMBG every four weeks until antepartum (n=77)	SMBG (n=77)
Wei et al (2016)[44,]	China	1	2011-2012	Pregnant women with gestational diabetes diagnosed between 24 and 28 wk of gestation; mean HbA1c level, 5.8%; mean age, 30 y	CGM (48- 721 on weekdays) (n=51)	SMBG (n=55)

BMI: Body mass index; CGM: continuous glucose monitoring; HbA1c: hemoglobin A_{1c}; RCT: randomized controlled trial; SMBG: self-monitored blood glucose.

Table 20. RCT Outcomes for CGM in Pregnant People With Gestational Diabetes

Study	Infant				Maternal	
	Large-for-Gestational Age, n (%)	Gestational Age at Delivery, wk	Severe Hypoglycemia, n (%)	Caesarean Section, n (%)	HbA1c Levels Before Delivery[a]	Severe Hypoglycemia
Lai et al (2023)[43,]						
N	124	NR	124	124	124	NR
CGM	5 (8)		1 (2)	34 (55)	Mean, 5.3%	
Control	5 (8)		1 (2)	36 (58)	Mean, 5.4%	
TE (95% CI)	1.00 (0.52 to 1.91)		RR=1.00 (0.25 to 4.04)	RR=0.94 (0.65 to 1.34)	NR	
p	1.0		1.0	.71	.60	
Wei et al (2016)[44,]						
N	106	106	106	106	NR	NR
CGM	18 (35)	Mean, 37.4	4 (8)	31 (60)	Mean, 5.5%	
Control	29 (53)	Mean, 37.5	7 (13)	38 (69)	Mean, 5.6%	
TE (95% CI)	NR	NR	NR	NR	NR	
p	.07	.92	.41	.37	.09	

Values are n (%) or as otherwise indicated.

CGM: continuous glucose monitoring; CI: confidence interval; HbA1c: hemoglobin A_{1c}; NR: not reported; RCT: randomized controlled trial; RR: relative risk; TE: treatment effect.
[a] N inconsistently reported for HbA1c outcome.
Tables 21 and 22 display notable limitations identified in the studies.

Table 21. Study Relevance Limitations of RCTs for CGM in Pregnant People With Gestational Diabetes

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Follow-Up[e]
Lai et al (2023)[43,]	4. Study population had relatively low HbA1c level 5. Study conducted entirely in China	4. Compliance with CGM not reported	4. Compliance with control not reported	1. Maternal hypoglycemia not reported	
Wei et al (2016)[44,]	4. Study population had relatively low HbA1c level 5. Study conducted entirely in China	4. Compliance with CGM not reported			

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
CGM: continuous glucose monitoring; HbA1c: hemoglobin A_{1c}; RCT: randomized controlled trial.
[a] Population key: 1. Intended use population unclear; 2. Clinical context is unclear; 3. Study population is unclear; 4. Study population not representative of intended use; 5. Enrolled study populations do not reflect relevant diversity.
[b] Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4.Not the intervention of interest.
[c] Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively.
[d] Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. No CONSORT reporting of harms; 4. Not establish and validated measurements; 5. Clinical significant difference not prespecified; 6. Clinical significant difference not supported.
[e] Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms.

Table 22. Study Design and Conduct Limitations of RCTs for CGM in Pregnant People With Gestational Diabetes

Study	Allocation[a]	Blinding[b]	Selective Reporting[c]	Data Completeness[d]	Power[e]	Statistical[f]
Lai et al (2023)[43,]	3. Not reported	1. Not blinded	2. Hierarchy of outcomes unclear in publication	1, 2. 15 (19%) participants in each group discontinued study and were not accounted for in analysis	1. No power calculations reported; primary outcome not specified in publication but listed in registration	
Wei et al (2016)[44,]	3. Not reported	1. Not blinded; chance of bias in clinical management	1. Registration not reported	5. Exclusions not well justified	1. No power calculations reported; primary outcome not specified	3, 4. Treatment effects and CIs not calculated

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
CGM: continuous glucose monitoring; CI: confidence interval; RCT: randomized controlled trial.
[a] Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias.
[b] Blinding key: 1. Not blinded to treatment assignment; 2. Not blinded outcome assessment; 3. Outcome assessed by treating physician.
[c] Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication.
[d] Data Completeness key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials).

[e] Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference.
[f] Statistical key: 1. Analysis is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event; 2. Analysis is not appropriate for multiple observations per patient; 3. Confidence intervals and/or p values not reported; 4.Comparative treatment effects not calculated.

Section Summary: Continuous Glucose Monitoring Use in Pregnant People With Gestational Diabetes

The 2 RCTs in women with gestational diabetes were conducted in China with the intervention starting in the second or third trimester and mean baseline HbA1c level less than 6.0%. The GlucoMOMS trial also included women with gestational diabetes. Trial reporting was incomplete; however, there were no differences between groups for most reported outcomes.

Continuous Glucose Monitoring Implanted Device

Clinical Context and Therapy Purpose

The purpose of an implantable CGM device is to provide a treatment option that is an alternative to or an improvement on existing therapies in individuals with diabetes.

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is individuals with type 1 or type 2 diabetes.

Interventions

One implantable CGM device (Eversense) is FDA cleared for use in the US. The Eversense Continuous Glucose Monitoring System is implanted in the subcutaneous skin layer and provides continuous glucose measurements over a 40 to 400 mg/dL range. The system provides real-time glucose values, glucose trends, and alerts for hypoglycemia and hyperglycemia and through a mobile application installed on a compatible mobile device platform. The Eversense CGM System is a prescription device indicated for use in adults (age 18 and older) with diabetes for up to 180 days. The device was initially approved as an adjunctive glucose monitoring device to complement information obtained from standard home blood glucose monitoring devices. Prescribing providers are required to participate in insertion and removal training certification.

Comparators

The following practice is currently being used to measure glucose levels: capillary blood sampling (finger stick) with blood glucose meters for self-monitoring.

Outcomes

The general outcomes of interest are a change in HbA1c levels, time spent in hypoglycemia, the incidence of hypoglycemic events, complications of hypoglycemia and QOL.

To assess short-term outcomes such as HbA1c levels, time spent in hypoglycemia, the incidence of hypoglycemic events, and complications of hypoglycemia, a minimum follow-up of 8 to 12 weeks is appropriate. To assess long-term outcomes such as QOL and maternal and infant outcomes, follow-up of 24 to 36 weeks would be appropriate.

Study Selection

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.

- To assess long-term outcomes and adverse effects, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded.

Review of Evidence

Randomized Studies

One trial of implantable CGM in people with diabetes has been published. Trial characteristics, results, and limitations for the RCTs are shown in Tables 23 to 26 and briefly described below.

Renard et al (2022) reported results of the multicenter France Adoption Randomized Clinical Trial (NCT03445065) comparing implantable Eversense real-time CGM (n=159) versus self-monitoring of blood glucose or intermittently scanned CGM (n=80) in individuals with type 1 or type 2 diabetes.[45,] Participants were adults, age 18 years and older, on multiple daily insulin injections or insulin pump. Participants were enrolled in 2 cohorts. Cohort 1 (n=149) included participants with type 1 or type 2 diabetes with HbA1c levels >8%. Cohort 2 (n=90) included participants with type 1 with time spent with glucose values below 70 mg/dL for more than 1.5 hours per day in the previous 28 days. The primary outcomes were changes in HbA1c at day 180 in cohort 1 and change in time spent with glucose below 54 mg/dL between days 90 and 120 in cohort 2. In cohort 1, there was no difference in HbA1c at day 180 (difference=-0.1; 95% CI, -0.4 to 0.1; p=.34) or in time in range (difference=-0.9; 95% CI, -6.7 to 4.8; p=.75). For cohort 2, the mean difference in time spent below 54 mg/dL between days 90 and 120 was statistically significant favoring implantable CGM (difference=-1.6% [23 minutes]; 95% CI, -3.1 to -0.1; p=.04). Six out of 239 (3%) participants experienced skin irritation and/or redness from sensor insertion; 5 (2%) reported itching or pruritus and 5 (2%) reported at least one hematoma formation. Results for the patient-reported outcomes were not provided, but the text indicated that there were 'no significant changes'.

Table 23. Key RCT Characteristics for implantable CGM in People With Diabetes

Study	Countries	Sites	Dates	Participants	Interventions	
					Active	*Comparator*
Renard et al (2022) [45,]	France	20	2018-2020	Adults, age ≥18 years, with type 1 or type 2 diabetes on multiple daily insulin injections or insulin pump. Cohort 1 (n=149) included participants with type 1 or type 2 diabetes with HbA1c levels >8%; 55% female; 87% type 1 diabetes; mean age, 43 y Cohort 2 (n=90) included participants with type 1 with time spent with glucose values <70 mg/dL for >1.5 hours per day in the previous 28 days; 28% female; mean age, 46 y	' Enabled' Eversense sensor; Not allowed to use any other CGM Cohort 1 n=97 Cohort 2 n=62	Blinded Eversense sensor; Continued using SMBG or intermittently-scanned CGM Cohort 1 n=52 Cohort 2 n=28

Table 24. Summary of Key RCT Results for implantable CGM in People With Diabetes

Study	HbA1c	Blood Glucose (SD) mg/dL	Hypoglycemic Episodes	Patient Reported Outcomes
Renard et al (2022) [Renard E, Riveline JP, Hanaire H, et al. Reduction.... 24(5): 859-867. PMID 34984786]				

Study	HbA1c	Blood Glucose (SD) mg/dL	Hypoglycemic Episodes	Patient Reported Outcomes
Cohort 1 (type 1 or type 2, high baseline HbA1c)	At day 180, primary outcome	Time below range (<54) between day 90 and 120		
N	149	149	149	NR
Implantable CGM	8.7 (1.1)	1.2 (2.0)	0	
Control	8.8 (1.0)	1.4 (1.8)	1	
Diff (95% CI)	-0.1 (-0.4 to 0.1)	-0.1 (-0.7 to 0.4)		'No difference'
p	.34	.68		
Cohort 2 (type 1, significant time with low glucose)	At day 180	Time below range (<54) between day 90 and 120; primary outcome		
N	90	90	90	NR
Implantable CGM	7.4 (0.9)	3.9 (3.1)	0	
Control	6.9 (1.0)	6.0 (5.3)	0	
Diff (95% CI)	0.1 (-0.2 to 0.4)	-1.6 (-3.1 to -0.1)		'No difference'
p	.62	.04		

Table 25. Study Relevance Limitations of RCTs for implantable CGM in People With Diabetes

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Follow-Up[e]
Renard et al (2022) [Renard E, Riveline JP, Hanaire H, et al. Reduction.... 24(5): 859-867. PMID 34984786]	5. Study conducted entirely in France; racial characteristics not reported			1. Percent of participants meeting target HbA1c goals not reported	1, 2. Follow-up limited to 180 days

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
CGM: continuous glucose monitoring; RCT: randomized controlled trial.
[a] Population key: 1. Intended use population unclear; 2. Clinical context is unclear; 3. Study population is unclear; 4. Study population not representative of intended use; 5. Enrolled study populations do not reflect relevant diversity.
[b] Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4.Not the intervention of interest.
[c] Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively.
[d] Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. No CONSORT reporting of harms; 4. Not establish and validated measurements; 5. Clinical significant difference not prespecified; 6. Clinical significant difference not supported.
[e] Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms.

Table 26. Study Design and Conduct Limitations of RCTs for implantable CGM in People With Diabetes

Study	Allocation[a]	Blinding[b]	Selective Reporting[c]	Data Completeness[d]	Power[e]	Statistical[f]
Renard et al (2022) [Renard E, Riveline JP, Hanaire H, et al. Reduction.... 24(5): 859-867. PMID 34984786]		1. Control arm described as 'blinded' but only participants in the implantable CGM arms were trained to use the system and were not allowed to use	2. Several outcomes reported as no change without numeric results	1. ITT analyses were reported. However, 50% of participants had primary outcome measurements taken outside of window in cohort 1. In	1. Assumptions for power calculations not given	3, 4. Numeric results not given for several outcome measures

Study	Allocation[a]	Blinding[b]	Selective Reporting[c]	Data Completeness[d]	Power[e]	Statistical[f]
		other CGM while participants in the control arm were allowed to use other CGM devices		cohort 2, 27% of participants had less than 70% of CGM data available for the primary outcome.		

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
CGM: continuous glucose monitoring; RCT: randomized controlled trial.
[a] Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias.
[b] Blinding key: 1. Not blinded to treatment assignment; 2. Not blinded outcome assessment; 3. Outcome assessed by treating physician.
[c] Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication.
[d] Data Completeness key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials).
[e] Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference.
[f] Statistical key: 1. Analysis is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event; 2. Analysis is not appropriate for multiple observations per patient; 3. Confidence intervals and/or p values not reported; 4.Comparative treatment effects not calculated.

Nonrandomized Studies

Data from 3 nonrandomized prospective studies (PRECISE, PRECISE II, AND PRECISION) were provided to the U.S. Food and Drug Administration (FDA) for the initial approval of Eversense as an adjunctive device.[46,47,] Expanded approval was granted in June 2019 and Eversense is now approved as a device to replace fingerstick blood glucose measurements for diabetes treatment decisions.[48,] Historical data from the system can be interpreted to aid in providing therapy adjustments. No new clinical studies were conducted to support the change in the indications for the device. The sponsor had previously performed clinical studies to establish the clinical measurement performance characteristics of the device, including accuracy across the claimed measuring range (40 to 400 mg/dL glucose), precision, claimed calibration frequency (every 12 hours), the wear period for the sensor (90 days), and performance of the alerts and notifications. This same clinical study information was used to support what the FDA considered a reasonable assurance of safety and effectiveness of the device for the replacement of fingerstick blood glucose monitoring for diabetes treatment decisions.

In 2022, Eversense was FDA approved for use up to 180 days. Approval was based on the PROMISE pivotal study, which was designed to assess the safety and accuracy of the 180-day device.[49,] PROMISE was a prospective, multicenter, unblinded, nonrandomized study of 181 adults with Type 1 (69.6%) and type 2 (30.4%) diabetes conducted at 8 sites in the U.S. Participants had diabetes for at least 1 year. Participants were heterogenous with regard to diabetes treatment: 50.8% were using a continuous insulin infusion pump, 35.9% multiple daily injections of insulin, 8.8% oral diabetes medications only, and 4.4% basal insulin or only 1 injection per day (4.4%). Accuracy of the device was evaluated by comparing CGM to glucose analyzer values during 10 clinic visits. Sensors were removed after day 180. The safety endpoint was the rate of device-related or sensor insertion/removal procedure-related serious adverse events. For primary sensors, the percent CGM readings within 20% of glucose analyzer values was 92.9%; the overall mean absolute relative difference was 9.1%. There were no serious adverse events related to the device or insertion/removal procedures. There were no unanticipated adverse events and the most frequently reported adverse events were dermatological (e.g. skin irritation). All primary sensors were successfully removed on the first attempt.

Multiple post-marketing registry studies of the Eversense device have been published (Tables 27 and 28). Sanchez et al (2019) reported glucometric and safety data on the first 205 patients in the U.S. to use the Eversense device for at least 90 days.[50,] Of the 205 patients, 62.9% reported having type 1 diabetes, 8.8% type 2 diabetes , and 28.3% were unreported; results were not reported separately by diabetes type. Diess et al (2019) reported safety outcomes for 3023 patients from 534 sites in Europe and South Africa who had used the device for 6 months or longer.[51,] There were no serious adverse events, and the most commonly reported adverse events were sensor site infection and skin irritation. Tweden et al (2019) reported accuracy and safety data from 945 patients in Europe and South Africa who used either the 90-day or 180 day Eversense system for 4 insertion-removal cycles.[52,] The percentage of patients using the 180-day system increased from cycle 1 to 4 as the device became more widely available (9%, 39%, 68% and 88% in cycles 1 to 4). There was no evidence of degradation of performance of the device over repeated insertion/removal cycles. Adverse events were not otherwise reported. Irace et al (2020) reported results of an uncontrolled study of 100 adults with type 1 diabetes at 7 centers in Italy who had the Eversense 180-day device inserted for the first time. Forty-five percent of participants were previous CGM users. Overall, HbA1c declined from a mean of 7.4% at baseline to 6.9% at 180 days (p<.0001). The greatest mean reduction was in the subgroup of participants were CGM naive. No serious device-related adverse events occurred. There were 2 device-related adverse events: A mild incision site infection in one participant and inability to remove the device on the first attempt in a second participant.

Limitations of the evidence base include limited direct comparisons to SMBG, lack of differentiation in outcomes for type 1 diabetes versus type 2 diabetes, and variability in reporting of trends in secondary glycemic measures. As a condition of approval, the Eversense sponsor is required to conduct a post-approval-study to evaluate the safety and effectiveness of the system compared to self-monitoring of blood glucose using a blood glucose meter in participants with either Type 1 or Type 2 diabetes (NCT04836546).[48,] The study is expected to be completed in March 2026.

Table 27. Postmarketing Studies of the Eversense Device- Characteristics

Study	Study Type	Country	Dates	Participants	Test/Treatment	Follow-Up
Deiss et al (2019)[51,]	Prospective, single-arm	Europe and South Africa	2016-2018	Adults (≥18 years) with T1D or T2D (% not reported) Consecutive patients who reached 4 sensor insertion/removal cycles Total N=3023; 6 months of use (N=969), 1 year of use (N=173)	Implanted CGM Single sensor (90-day or 180-day)	Up to 1 year
Sanchez et al (2019)[50,]	Prospective, single-arm	United States	2018-2019	Consecutive participants who reached a 90-day wear period of the device (62.9% T1D, 8.8% T2D, 28.3% unreported) (N=205)	Implanted CGM	90 days
Tweden et al (2019)[52,]	Prospective, single-arm	Europe and South Africa	2016-2019	Adults with T1D or T2D (% not known) for whom the Eversense CGM System was prescribed and inserted by their health care provider across approximately 1000 centers in Europe and South Africa (N=945)	Implanted CGM 90-day system or 180-day system	4 insertion-removal cycles
Irace et al (2020)[53,] NCT04160156	Prospective, single-arm	Italy	2018-2019	Adults (≥18 years) with T1D; 56% used insulin pumps and 44% used multiple daily injections of insulin; 45% wer previous CGM users. Mean HbA1c 7.4% (SD 0.92%)	Implanted CGM 180-day system	180 days

CGM: continuous glucose monitoring; HbA1c: hemoglobin $A_{1c;}$ SD: standard deviation; T1D: type 1 diabetes; T2D: type 2 diabetes.

Table 28. Postmarketing Studies of the Eversense Device- Results

Study Efficacy Outcomes	Efficacy Results	Adverse Events
Deiss et al (2019)[51,]		N=3023
	NR (safety only)	133 adverse events (85 procedure-related, 22 device-related, 6 drug-related, 4 device/procedure related; 16 not related) No related serious adverse events through 4 insertion/removal cycles. infection (n=29 patients); adhesive patch irritation (n=20 patients); unsuccessful first removal attempt (n=23 patients)
Sanchez et al (2019)[50,]	N=205	N=205
MARD (glucose range 40-400 mg/dl)	11.2% (SD 11.3%, median 8.2%).	10 (5%) transient skin irritation, redness, and/or swelling. 4 (2%) mild infection, 3 (1.5%) hypoglycemia that was self-treated, 4 (2%) failure to remove the sensor on the first attempt, and 5 (2.5%) skin irritation due to the adhesive
Mean SG (mg/dL)	161.8 Median 157.2 (IQR 138.4 to 178.9)	
% SG values in hypoglycemia (<54 mg/dL), 24-hour period	1.2% (18.0 minutes)	
% SG values in hypoglycemia (<54 mg/dL), nighttime	1.7%	
TIR, 24-hour period	62.3% (~15 hours)	
TIR, nighttime	61.8%	
Time in mild hyperglycemia, 24-hour period	21.9%	
Time in mild hyperglycemia, nighttime	21.5%	
Time in significant hyperglycemia, 24-hour period	11.6%	
Time in significant hyperglycemia, nighttime	12.1%	
Tweden et al (2019)[52,]		
MARD (glucose range 40-400 mg/dl)	Mean 11.5% to 11.9% during each sensor cycle	No evidence of degradation of performance from the repeated insertion and removal procedures occurring in approximately the same subcutaneous tissue of the body. Adverse events otherwise not reported.
Mean SG (mg/dL)	156.5 to 158.2 mg/dL across 4 sensor cycles	
% SG values in significant hypoglycemia (<54 mg/dL), 24-hour period	1.1% to 1.3% (16 to 19 minutes)	
% SG values in significant hypoglycemia (<70 mg/dL), 24-hour period	4.6% to 5.0% (66 to 72 minutes)	
TIR, 24-hour period	63.2% to 64.5% (910 to 929 minutes)	
Time in hyperglycemia (>180-250 mg/dL), 24-hour period	22.8% to 23.2% (328 to 334 minutes)	
Time in significant hyperglycemia (>250 mg/dL), 24-hour period	8.1% to 8.8% (117 to 127 minutes)	
Irace et al (2020)[53,]		
HbA1c change from baseline % (SD)	7.4 % (0.92) to 6.9 (0.76)	No serious device-related adverse events occurred. There were 2 device-related adverse events: A mild incision site infection in one participant and inability to remove the device on the first attempt in a second participant.
Mean change from baseline to 180 days, % (SD)	0.43 (0.69); p<.001	
Time in range change from baseline	63% to 69%	
Mean change from baseline to 18 days	6%; p<.0001	

CGM: continuous glucose monitoring; HbA1c: hemoglobin $A_{1c;}$ IQR: interquartile range; MARD: mean absolute relative difference; NR: not reported; SD: standard deviation; SG: sensor glucose; TIR: time in range.

Section Summary: Continuous Glucose Monitoring Implanted Device for Long-Term Use

One RCT compared implantable CGM with control (self-monitoring of blood glucose or intermittently scanned CGM). The RCT was conducted in France and enrolled participants in 2 cohorts; cohort 1 (n=149) included participants with type 1 or type 2 diabetes with HbA1c >8.0% while cohort 2 (n=90) included participants with type 1 diabetes with time spent with glucose values below 70 mg/dL for more than 1.5 hours per day in the previous 28 days. In cohort 1, there was no difference in mean HbA1c, time in range, or patient-reported outcomes at day 180. In cohort 2, the mean difference in time spent below 54 mg/dL between days 90 and 120 was statistically significant favoring implantable CGM (difference=-1.6% [23 minutes]; 95% CI, -3.1 to -0.1; p=.04). There were no differences in patient reported outcomes.

Nonrandomized prospective studies and postmarketing registry studies assessed the accuracy and safety of an implanted glucose monitoring system that provides CGM for up to 4 insertion/removal cycles as an adjunct to home glucose monitoring devices. Accuracy measures included the mean absolute relative difference between paired samples from the implanted device and a reference standard blood glucose measurement. The accuracy tended to be lower in hypoglycemic ranges. The initial approval of the device has been expanded to allow the device to be used for glucose management decision making. The same clinical study information was used to support what the FDA considered a reasonable assurance of safety and effectiveness of the device for the replacement of fingerstick blood glucose monitoring for diabetes treatment decisions. In February 2022, the FDA expanded approval of the device for use up to 180 days. Approval was based on the PROMISE pivotal clinical trial, which assessed accuracy and safety but not glycemic outcomes. Limitations of the evidence base include lack of direct comparisons to SMBG, lack of differentiation in outcomes for type 1 diabetes versus type 2 diabetes, and variability in reporting of trends in secondary glycemic measures.

Supplemental Information

The purpose of the following information is to provide reference material. Inclusion does not imply endorsement or alignment with the evidence review conclusions.

Clinical Input From Physician Specialty Societies and Academic Medical Centers

While the various physician specialty societies and academic medical centers may collaborate with and make recommendations during this process, through the provision of appropriate reviewers, input received does not represent an endorsement or position statement by the physician specialty societies or academic medical centers, unless otherwise noted.

2019 Input

Clinical input was sought to help determine whether the use of continuous or intermittent monitoring of glucose in the interstitial fluid would provide a clinically meaningful improvement in net health outcome and whether the use is consistent with generally accepted medical practice. In response to requests, clinical input was received from 3 respondents, including 3 physician-level responses identified through 1 specialty society, including 2 physicians with academic medical center affiliations.

Type 1 Diabetes

For individuals who have type 1 diabetes who receive short-term glucose monitoring, clinical input supports that this use provides a clinically meaningful improvement in net health outcome and is consistent with generally accepted medical practice when used in specific situations such as poor control of Type 1 diabetes despite the use of best practices and to help determine basal insulin levels prior to insulin pump initiation.

Type 2 Diabetes

For individuals who have type 2 diabetes who do not require insulin who receive long-term continuous glucose monitoring (CGM), clinical input does not support a clinically meaningful improvement in net health outcome and does not indicate this use is consistent with generally accepted medical practice.

For individuals with type 2 diabetes who are willing and able to use the device and have adequate medical supervision and who experience significant hypoglycemia on multiple daily doses of insulin or an insulin pump in the setting of insulin deficiency who receive long-term continuous glucose monitoring, clinical input supports that this use provides a clinically meaningful improvement in net health outcome and is consistent with generally accepted medical practice.

For individuals with type 2 diabetes who require multiple daily doses of insulin who receive short-term CGM, clinical input supports that this use provides a clinically meaningful improvement in net health outcome and is consistent with generally accepted medical practice when used in specific situations such as poor control of diabetes despite use of best practices and to help determine basal insulin levels prior to insulin pump initiation.

Further details from clinical input are included in the Appendix.

Practice Guidelines and Position Statements

Guidelines or position statements will be considered for inclusion in 'Supplemental Information' if they were issued by, or jointly by, a US professional society, an international society with US representation, or National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

American Association of Clinical Endocrinologists

In 2022, the American Association of Clinical Endocrinology (AACE) published clinical practice guideline for developing diabetes care plans and made the following recommendations (level of evidence) on CGM:[54,]

- "All persons who use insulin should use continuous glucose monitoring (CGM) or perform blood glucose monitoring (BGM) a minimum of twice daily and ideally before any insulin injection." **(Grade A; Best Evidence Level 1)**
- "Real-time continuous glucose monitoring (rtCGM) or intermittently scanned continuous glucose monitoring (isCGM) is recommended for all persons with T1D, regardless of insulin delivery system, to improve A1C levels and to reduce the risk for hypoglycemia and DKA." **(Grade A; Best Evidence Level 1)**
- "rtCGM or isCGM is recommended for persons with T2D who are treated with insulin therapy, or who have high risk for hypoglycemia and/or with hypoglycemia unawareness." **(Grade A; Best Evidence Level 1)**

In 2021, the American Association of Clinical Endocrinology (AACE) published recommendations on the use of advanced technology in the management of diabetes and made the following recommendations (level of evidence) on CGM:[55,]

- CGM is strongly recommended for all persons with diabetes treated with intensive insulin therapy, defined as 3 or more injections of insulin per day or the use of an insulin pump. (**Grade A; High Strength of Evidence**)
- CGM is recommended for all individuals with problematic hypoglycemia (frequent/severe hypoglycemia, nocturnal hypoglycemia, hypoglycemia unawareness).(**Grade A; Intermediate-High Strength of Evidence**)
- CGM is recommended for children/adolescents with T1D. (**Grade A; Intermediate-High Strength of Evidence**)

- CGM is recommended for pregnant women with T1D and T2D treated with intensive insulin therapy. (**Grade A; Intermediate-High Strength of Evidence**)
- CGM is recommended for women with gestational diabetes mellitus (GDM) on insulin therapy. (**Grade A; Intermediate Strength of Evidence**)
- CGM may be recommended for women with GDM who are not on insulin therapy. (**Grade B; Intermediate Strength of Evidence**)
- CGM may be recommended for individuals with T2D who are treated with less intensive insulin therapy. (**Grade B; Intermediate Strength of Evidence**)

American Diabetes Association

The American Diabetes Association (2023) "Standards of Medical Care in Diabetes[56,]" made the following recommendations (**level of evidence**) on CGM devices:

- "Real-time CGM (**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."
- "Real-time CGM (**A**) or intermittently scanned continuous glucose monitoring (**C**) should be offered 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."
- "Real-time CGM (**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."
- "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 the devices safely (either by themselves or with a caregiver). The choice of device should be made based on the individual's circumstances, preferences, and needs." **(E)**
- When used as an adjunct to pre- and postprandial blood glucose monitoring, CGM can help to achieve A1c targets in diabetes and pregnancy **(B).**
- Periodic use of real-time or intermittently scanned cCGM or use of professional CGM can be helpful for diabetes management in circumstances where continuous use of CGM is not appropriate, desired, or available **(C)**.

National Institute for Health and Care Excellence

In 2022, the National Institute for Health and Care Excellence (NICE) updated its guidance on management of type 1[57,] and type 2[58,] diabetes. The guidance included the following updated recommendations on CGM (refer to source documents for complete guidance):

Type 1 Diabetes

- "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. "

"When choosing a (CGM) device:

- use shared decision making to identify the person's needs and preferences, and offer them an appropriate device
- if multiple devices meet their needs and preferences, offer the device with the lowest cost"[57,]

Type 2 Diabetes

"Offer intermittently scanned continuous glucose monitoring (isCGM, commonly referred to as 'flash') to adults with type 2 diabetes on multiple daily insulin injections if any of the following apply:

- they have recurrent hypoglycaemia or severe hypoglycaemia
- they have impaired hypoglycaemia awareness
- they have a condition or disability (including a learning disability or cognitive impairment) that means they cannot self-monitor their blood glucose by capillary blood glucose monitoring but could use an isCGM device (or have it scanned for them)
- they would otherwise be advised to self-measure at least 8 times a day."

"Offer isCGM to adults with insulin-treated type 2 diabetes who would otherwise need help from a care worker or healthcare professional to monitor their blood glucose."

"Consider real-time continuous glucose 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."[58,]

The guidance and accompanying evidence review do not specifically mention implantable CGM devices.

Endocrine Society

The Endocrine Society (2022) published clinical practice guidelines of management of individuals at high risk of hypoglycemia and included the following recommendations on CGM:[59,]

- We recommend CGM rather than self-monitoring of blood glucose (SMBG) by fingerstick for patients with type 1 diabetes (T1D) receiving multiple daily injections (MDIs).
- We suggest real-time continuous glucose monitoring CGM be used rather than no CGM for outpatients with type 2 diabetes (T2D) who take insulin and/or sulfonylureas (SUs) and are at risk for hypoglycemia.

The Endocrine Society (2016) published clinical practice guidelines that included the following recommendations on CGM[60,]:

6. "Real-time continuous glucose monitors in adult outpatients
   6.1 We recommend real-time continuous glucose monitoring (RT-CGM) devices for adult patients with T1DM [type 1 diabetes mellitus] who have A1C levels above target and who are willing and able to use these devices on a nearly daily basis.
   6.2 We recommend RT-CGM devices for adult patients with well-controlled T1DM who are willing and able to use these devices on a nearly daily basis.
   Use of continuous glucose monitoring in adults with type 2 diabetes mellitus [T2DM]
   6.3 We suggest short-term, intermittent RT-CGM use in adult patients with T2DM (not on prandial insulin) who have A1C levels ≥7% and are willing and able to use the device."

U.S. Preventive Services Task Force Recommendations

Not applicable.

Medicare National Coverage

In January 2017, the Centers for Medicare & Medicaid Services (CMS) ruled that CGM devices (therapeutic CGMs) approved by the U.S. Food and Drug Administration (FDA) that can be used to make treatment decisions are considered durable medical equipment.[61,] A CGM is considered a therapeutic CGM if it is approved by the FDA for use in place of a blood glucose monitor for making diabetes treatment decisions such as changes in diet and insulin dosage. Initially, CMS did not consider the smartphone application as a DME component and did allow payment for that part of the CGM system. Subsequently, in June 2018, CMS made an announcement that Medicare's published coverage policy for CGMs will be modified to support the use of CGMs in conjunction with a

smartphone, including the important data sharing function they provide for patients and their families.[62,] Currently marketed therapeutic CGM systems are included in Table 1.

In 2020, Medicare assigned relative value units to the insertion, removal and removal/reinsertion codes uses for provision of the implantable glucose sensor device.

Ongoing and Unpublished Clinical Trials

Some currently ongoing and unpublished trials that might influence this review are listed in Table 29.

Table 29. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT03981328	The Effectiveness of Real Time Continuous Glucose Monitoring to Improve Glycemic Control and Pregnancy Outcome in Patients With Gestational Diabetes Mellitus	372	Dec 2023
NCT03908125[a]	A Post- Approval Study to Evaluate the Long-term Safety and Effectiveness of the Eversense® Continuous Glucose Monitoring (CGM) System	273 (Actual enrollment)	Mar 2023
NCT04836546	A Post Approval Study to Evaluate the Safety and Effectiveness of the Eversense® Continuous Glucose Monitoring (CGM) System Used Non-adjunctively	925	Mar 2026
NCT05131139	Enhance Study: A Prospective, Multicenter Evaluation of Accuracy and Safety of the Eversense CGM System With Enhanced Features	350	Sep 2025
Unpublished			
NCT04535830	The Effectiveness of Flash Glucose Monitoring System on Glycemic Control in Patients With New-onset Type 2 Diabetes#A Randomized Controlled Trial	200	Sep 2021 (unknown status)
NCT03445065[a]	Benefits of a Long Term Implantable Continuous Glucose Monitoring System for Adults With Diabetes - France Randomized Clinical Trial	239	Aug 2020

NCT: national clinical trial.
[a] Denotes industry-sponsored or cosponsored trial.

Appendix 1

Clinical Input

Respondents

Clinical input was provided by the following specialty societies and physician members identified by a specialty society or clinical health system:

- Chaitanya Mamillapalli, MD, MRCP, FAPCR, Endocrinology, Springfield Clinic, identified by American Association of Clinical Endocrinologists (AACE)**
- Vijay Shivaswamy, MBBS, Endocrinology, University of Nebraska Medical Center and Omaha Veterans Administration, identified by AACE
- Janet B. McGill, MD, Endocrinology, Washington University School of Medicine, identified by AACE**

* Indicates that no response was provided regarding conflicts of interest related to the topic where clinical input is being sought.

** Indicates that conflicts of interest related to the topic where clinical input is being sought were identified by this respondent (see Appendix).

Clinical input provided by the specialty society at an aggregate level is attributed to the specialty society. Clinical input provided by a physician member designated by a specialty society or health system is attributed to the individual physician and is not a statement from the specialty society or

health system. Specialty society and physician respondents participating in the Evidence Street® clinical input process provide a review, input, and feedback on topics being evaluated by Evidence Street. However, participation in the clinical input process by a specialty society and/or physician member designated by a specialty society or health system does not imply an endorsement or explicit agreement with the Evidence Opinion published by BCBSA or any Blue Plan.

CI - Objective

Clinical input was sought to help determine whether the use of a continuous or intermittent monitoring of glucose in interstitial fluid in individuals with diabetes would provide a clinically meaningful improvement in net health outcome and whether the use is consistent with generally accepted medical practice.

The following PICO applies to this request.

Populations	Interventions	Comparators	Outcomes
Individuals: • **With type 1 diabetes**	Interventions of interest are: • Short-term (intermittent) glucose monitoring	Comparators of interest are: • Self-monitoring of blood glucose	Relevant outcomes include: • Symptoms • Morbid events • Quality of life • Treatment-related morbidity
Individuals: • **With type 2 diabetes**	Interventions of interest are: • Long-term (continuous) glucose monitoring	Comparators of interest are: • Self-monitoring of blood glucose	Relevant outcomes include: • Symptoms • Morbid events • Quality of life • Treatment-related morbidity
Individuals: • **With type 2 diabetes**	Interventions of interest are: • Short-term (intermittent) glucose monitoring	Comparators of interest are: • Self-monitoring of blood glucose	Relevant outcomes include: • Symptoms • Morbid events • Quality of life • Treatment-related morbidity

Ratings

Clinical Indication	Respondent	Identified by	Confidence Level That Clinical Use Expected to Provide Clinically Meaningful Improvement in Net Health Outcome: Yes or No	NO: High 5	4	Intermediate 3	2	Low 1	YES: Low 1	2	Intermediate 3	4	High 5	Confidence Level that Clinical Use is Consistent with Generally Accepted Medical Practice: Yes or No	NO: High 5	4	Intermediate 3	2	Low 1	YES: Low 1	2	Intermediate 3	4	High 5
Use of short-term (intermittent) glucose monitoring for individuals with type 1 diabetes which is poorly controlled[1], despite current use of best practices and who are willing and able to use the device.	Dr. Mamillapalli**	AACE	Yes									■		Yes										■
	Dr. Shivaswamy	AACE	Yes						■					Yes						■				
	Dr. McGill**	AACE	No			■								NR										
Use of short-term (intermittent) glucose monitoring for individuals with type 1 diabetes prior to insulin pump initiation to determine basal insulin levels and who are willing and able to use the device.	Dr. Mamillapalli**	AACE	Yes									■		Yes										■
	Dr. Shivaswamy	AACE	Yes								■			Yes								■		
	Dr. McGill**	AACE	No			■								NR										
Use of long-term (continuous) glucose monitoring for individuals with type 2 diabetes who are insulinopenic and require multiple daily injections of insulin but who are poorly controlled[2] despite use of best practices and who are willing and able to use the device.	Dr. Mamillapalli**	AACE	Yes									■		Yes										■
	Dr. Shivaswamy	AACE	Yes									■		Yes									■	
	Dr. McGill**	AACE	Yes										■	NR										
Use of short-term (intermittent) glucose monitoring for individuals with type 2 diabetes who are insulinopenic and require multiple daily injections of insulin but who are poorly controlled[2] despite use of best practices and who are willing and able to use the device.	Dr. Mamillapalli**	AACE	Yes									■		Yes									■	
	Dr. Shivaswamy	AACE	Yes										■	Yes										■
	Dr. McGill**	AACE	No			■								NR										
Use of short-term (intermittent) glucose monitoring for individuals with type 2 diabetes who are insulinopenic and require multiple daily injections of insulin prior to insulin pump initiation to determine basal insulin levels and who are willing and able to use the device.	Dr. Mamillapalli**	AACE	Yes									■		Yes									■	
	Dr. Shivaswamy	AACE	Yes										■	Yes										■
	Dr. McGill**	AACE	No			■								NR										

[1] Type 1 diabetes which is poorly controlled includes the following clinical situations: unexplained hypoglycemic episodes, hypoglycemic unawareness, suspected postprandial hyperglycemia, and recurrent diabetic ketoacidosis.
[2] Type 2 diabetes which is poorly controlled includes the following clinical situations: unexplained hypoglycemic episodes, hypoglycemic unawareness, and persistent hyperglycemia and A1C levels above target.
** Indicates that conflicts of interest related to the topic where clinical input is being sought were identified by this respondent (see Appendix).
AACE: American Association of Clinical Endocrinologists; NR: No response

* Indicates that no response was provided regarding conflicts of interest related to the topic where clinical input is being sought.

** Indicates that conflicts of interest related to the topic where clinical input is being sought were identified by this respondent (see Appendix).

Detailed Responses

Respondent Profile

#	Physician Name	Degree	Institutional Affiliation	Clinical Specialty	Board Certification and Fellowship Training
Identified by American Association of Clinical Endocrinologists					
1	Chaitanya Mamillapalli	MD, MRCP, FAPCR	Springfield Clinic	Endocrinology	Endocrinology and Internal Medicine, Fellowship in Endocrinology
2	Vijay Shivaswamy	MBBS	University of Nebraska Medical Center and Omaha Veterans Administration	Endocrinology	Endocrinology
3	Janet B. McGill	MD	Washington University School of Medicine	Endocrinology	Endocrinology, Diabetes and Metabolism

Respondent Conflict of Interest Disclosure

#	1) Research support related to the topic where clinical input is being sought		2) Positions, paid or unpaid, related to the topic where clinical input is being sought		3) Reportable, more than $1,000, healthcare-related assets or sources of income for myself, my spouse, or my dependent children related to the topic where clinical input is being sought		4) Reportable, more than $350, gifts or travel reimbursements for myself, my spouse, or my dependent children related to the topic where clinical input is being sought	
	YES/NO	Explanation	YES/NO	Explanation	YES/NO	Explanation	YES/NO	Explanation
1	Yes	Our team has research grant approved from Abott diabetes care for the project "Impact of Joint Utilization of the FreeStyle Libre Flash Glucose Monitoring System and Flairz Health App on Glycemic Control in Patients with Type 2 Diabetes". This study will evaluate the concurrent use of the Abbott FreeStyle Libre Flash personal CGM and Flairz diabetes app on glycemic control for patients with type 2 diabetes mellitus requiring basal and prandial insulin for treatment	No		No		No	
2	No		No		No		No	
3	Yes	Current studies include WISDM (Wireless Innovation for Seniors with Diabetes Mellitus) and MOBILE (CGM in T2DM using basal insulin). Also Medtronic 670G study. Past studies include DIAMOND.	No		Yes	Intermittent speaker for Dexcom; grant funding from Dexcom and Medtronic	Yes	Travel to speaker training meeting and to investigator meeting for WISDM this year.

Individual physician respondents answered at individual level. Specialty Society respondents provided aggregate information that may be relevant to the group of clinicians who provided input to the Society-level response. NR = not reported

Questions and Responses

1. We are seeking your opinion on whether using the interventions for the below indications provide a clinically meaningful improvement in net health outcome. Please respond based on the evidence and your clinical experience. Please address these points in your response:
    - Relevant clinical scenarios (e.g., a chain of evidence) where the technology is expected to provide a clinically meaningful improvement in net health outcome;
    - Specific outcomes that are clinically meaningful;
    - Any relevant patient inclusion/exclusion criteria or clinical context important to consider in identifying individuals for this indication; and
    - Supporting evidence from the authoritative scientific literature (please include PMID).

#	Indications	Rationale-CI
1	Use of short-term	Short term CGM trial for 1-2 weeks is a common practice among endocrinologists in the following situations:

#	Indications	Rationale-CI
	(intermittent) glucose monitoring for individuals with type 1 diabetes	• In patients who has frequent hypoglycemia episodes • In patients with discrepancy between A1c and Self monitored blood glucose data • Uncontrolled diabetes • To monitor the trends of hyperglycemia and hypoglycemia to guide insulin dosing decisions • To screen for occult hypoglycemia episodes in patients with hypoglycemic awareness • Preoperative optimization of glucose control before surgery • Post-operative optimization of glucose control after surgery • Basal Insulin titration with new insulin pump starts • Patients who have recurrent DKAs • During pregnancy and to optimize glucose levels in the preconception period I respectfully disagree with the statement "Also, many of the trials of intermittent monitoring have included additional interventions to optimize glucose control (e.g., education, lifestyle modifications)." Outcome of CGMS studies should be studied in combination with interventions, as just measuring glucose data without making an intervention would not be successful.
2	Use of short-term (intermittent) glucose monitoring for individuals with type 1 diabetes	No comments. Agree with analysis
3	Use of short-term (intermittent) glucose monitoring for individuals with type 1 diabetes	Evidence is not only limited regarding short-term intermittent glucose monitoring, but the GOLD study clearly showed that when patients who have used long-term monitoring are returned to fingerstick glucose testing, their HbA1c increases back to the starting level and gains have been lost. While there are many factors driving high HbA1c in persons with T1DM, fear of hypoglycemia is the most commonly stated reason by my patients. Perkins et al recently reported that the strongest risk factor for macroalbuminuria or reduced eGFR in persons with T1DM in the DCCT/EDIC cohort is lifetime mean HbA1c, HR 1.952 per 1% higher level (95% CI 1.714 -2.223). • Perkins BA, Bebu I, de Boer IH, et al. Risk Factors for Kidney Disease in Type 1 Diabetes. Diabetes Care. 2019 42(5):883-890. PMID 30833370 Reducing glycemic burden safely requires the use of continuous glucose monitoring in the vast majority of patients. Baseline CGM data from the WISDM study (unpublished) uncovered an alarming rate of hypoglycemia in persons over the age of 60 with T1DM (unpublished data). The WISDM study will be presented at ADA and published thereafter. Long-term use of CGM in persons who are insulin deficient and require life-sustaining exogenous insulin is necessary for both safety to help achieve glycemic targets to prevent long-term complication. Short-term use of CGM is of modest benefit in persons with T1DM, may be helpful for adjusting insulin doses, but not for prevention of hypoglycemia or reduction of complications.
1	Use of long-term (continuous) glucose monitoring for individuals with type 2 diabetes	1. Review states "Four of the 6 RCTs of CGM in type 2 diabetes reported a statistically significant larger decrease in HbA1c levels with CGM than with control. No trials reported on follow-up beyond 6 months. Thus, the effect of CGM on outcomes related to diabetic complications is unknown." I respectfully disagree with the above statement. o It is important to note that the patients enrolled in this clinical trials have advanced diabetes with the duration of type 2 diabetes in the 8-21 years range. It is a challenge to improve glycemic control in this group, despite which CGM use in this population was associated with a meaningful improvement in A1c. o The short duration of studies did not allow for the evaluation of long-term outcomes, but one can extrapolate from the diabetes outcome clinical trials,

#	Indications	Rationale-CI

that the A1c improvements will help with the prevention of diabetes complications.

2. Additional efficacy studies which have demonstrated meaningful improvements in type 2 diabetes patients
    - Anjana RM, Kesavadev J, Neeta D, et al. A Multicenter Real-Life Study on the Effect of Flash Glucose Monitoring on Glycemic Control in Patients with Type 1 and Type 2 Diabetes. Diabetes Technol Ther. 2017;19(9):533-540. PMID: 28930495

FREESTYLE LIBREPRO™ FLASH GLUCOSE MONITORING (FCGM) IN BOTH TYPE1 AND TYPE

25072 patients with diabetes (Both Type 1 and Type 2) who had an A1c ≥7%. Overall, the magnitude of reduction in the intervention group was 1% compared to 0.7% in the control group P < 0.001). The overall reduction in A1c among cases was higher in T2D (9.2% to 8.3%) compared with T1D (9.6% to 9.4%);

- Yaron M, Roitman E, Aharon-Hananel G, et al. Effect of Flash Glucose Monitoring Technology on Glycemic Control and Treatment Satisfaction in Patients With Type 2 Diabetes. Diabetes Care. 2019; pii:dc180166. [Epub ahead of print] PMID 31036546

FLASH GLUCOSE MONITORING (FGM) SYSTEM IN PATIENTS WITH TYPE 2 DIABETICS.

The changes in HbA1c were −0.82% (9 mmol/mol) vs −0.33% (3.6 mmol/mol) in the intervention and control group, respectively (P = 0.005); 68.6% of the patients in the intervention group had their HbA1c reduced by ≥0.5% (5.5 mmol/mol) compared with 30.2% in the control group (P < 0.001), 39.2% had their HbA1creduced by ≥1.0% (10.9 mmol/mol) vs 18.6% in the control group (P = 0.0023) without an increased frequency of hypoglycemia. Satisfaction using the FGM system was high. The intervention group found treatment was more flexible (P = 0.019) and would recommend it to their counterparts (P = 0.023).

3. CGM Improves patient adherence to the ADA recommended guidelines for glucose measurements
    - American Diabetes Association. Standards of medical care in diabetes – 2018. Diabetes Care. 2018. p. 41.

In patients on intensive insulin treatment, ADA recommends checking glucose levels, but the frequency of blood glucose checking is suboptimal in the 2.6 range. The underlying cause for this is multifactorial 1. pain, 2. invasiveness 3. inconvenience, and 4. social stigma of finger stick glucose checks

CGM addresses these drawbacks and will help with improving the frequency of glucose checks.

- Dunn TC, Xu Y, Hayter G et al. Real-world flash glucose monitoring patterns and associations between self-monitoring frequency and glycaemic measures: A European analysis of over 60 million glucose tests. Diabetes Res Clin Pract. 2018 Mar;137:37-46. PMID 29278709

Patient performed average of 16.3 scans/day in a study involving Flash Glucose CGM. Higher A1c reduction was achieved with higher frequency of scans.

4. Use of alternative metrics other than A1C

Recent studies have demonstrated glycemic variability as an independent risk factor for diabetes complications.

- Monnier L, Mas E, Ginet C, et al. Activation of oxidative stress by acute glucose fluctuations compared with sustained chronic hyperglycemia in patients with type 2 diabetes. JAMA 2006;295:1681–1687. PMID: 16609090
- Ceriello A, Esposito K, Piconi L, et al. Oscillating glucose is more deleterious to endothelial function and oxidative stress than mean glucose in normal and type 2 diabetic patients. Diabetes 2008;57:1349–1354. PMID: 18299315
- Chang CM, Hsieh CJ, Huang JC, et al. Acute and chronic fluctuations in blood glucose levels can increase oxidative stress in type 2 diabetes mellitus. Acta Diabetol 2012;49(Suppl. 1): S171–S177. PMID: 22547264

Use of CGM was associated with decrease in glycemic variability

- Haak T, Hanaire H, Ajjan R et al. Flash Glucose-Sensing Technology as a Replacement for Blood Glucose Monitoring for the Management of Insulin-Treated Type 2 Diabetes:

#	Indications	Rationale-CI
		a Multicenter, Open-Label Randomized Controlled Trial. Diabetes Ther (2017 Feb) 8(1):55-73. PMID: 28000140 5. Hypoglycemia outcomes. In 2009 Hypoglycemia hospitalization costs in the USA was over 4.7 billion dollars in the US. (248,422 T2 diabetes hospitalizations and 20,839 Type 1 diabetes) o Singh G, Mithal A, Mannalithara A, et al. Hospitalisations due to severe hypoglycaemia in patients with type 2 diabetes: a US national perspective. Abstract accessible at URL: https://distribute.m-anage.com/check.pic?path=events%5C176%5Cabstract%5C25381%5C343775_628.pdf Use of CGM has been associated with reduction of hypoglycemia episodes. In the REPLACE trail Use of Flash CGM has been associated with reduction in hypoglycemia episodes. Time in hypoglycemia: • <70 mg/dL) reduced by 0.47 ± 0.13 h/day [mean ± SE (p = 0.0006)] 43% reduction • <55 mg/dL) reduced by 0.22 ± 0.07 h/day (p = 0.0014) for intervention participants compared with controls; 53% reduction • <45 mg/dL reduced by (−0.14 ± 0.04 h/day) 64% reduction • Nocturnal hypoglycemia 70mg/dL reduced by 54% (−0.29 ± 0.08 h per 7 h) for intervention participants compared with control (p = 0.0001). • Haak T, Hanaire H, Ajjan R et al. Flash Glucose-Sensing Technology as a Replacement for Blood Glucose Monitoring for the Management of Insulin-Treated Type 2 Diabetes: a Multicenter, Open-Label Randomized Controlled Trial. Diabetes Ther (2017 Feb) 8(1):55-73. PMID: 28000140
2	Use of long-term (continuous) glucose monitoring for individuals with type 2 diabetes	Use of Flash GM has shown reduction in hypoglycemia incidence. Use of Flash GM in type 2 DM on multi dose insulin regimen is widely covered by Medicare and VA facilities. A provision could be made to cover the Flash/Intermittent GM for type 2 DM on multi dose insulin regimen.
3	Use of long-term (continuous) glucose monitoring for individuals with type 2 diabetes	Persons with T2DM have highly variable physiology and treatment requirements. Some patients are highly insulin deficient, require physiologic insulin replacement, and are at risk for both severe hyperglycemic and hypoglycemic events. Patients with T2DM who require frequent glucose monitoring to adjust insulin therapy benefit from CGM in a similar manner to persons with T1DM. Persons at higher risk of hypoglycemia may benefit from long-term CGM. The data both less and less compelling for patients who do not require intensified insulin therapy. This group includes those who take basal insulin in addition to non-insulin therapies, and those who take only non-insulin medications for control of their diabetes. While the major problem is hyperglycemia and not hypoglycemia, CGM may be a cost-effective way to improve HbA1c in those not at goal, even reduce medication use. Unfortunately, data for use as an adjunct to lifestyle management is limited. Chehregosha and colleagues discuss the limitations of HbA1c, and greater utility of the metric, glucose management indicator (GMI, previously also known as eA1c) in the management of persons with T2DM. • Chehregosha H, Khamseh ME, Malek M, et al. A View Beyond HbA1c: Role of Continuous Glucose Monitoring. Diabetes Ther. 2019 Jun;10(3):853-863. PMID 31037553 Long-term use of CGM should be considered in patients whose diagnostic CGM shows discordance with HbA1c, those at risk for hypoglycemia, those on intensified insulin regimens and those who have achieved proven benefit from short-term CGM.
1	Use of short-term (intermittent) glucose monitoring for	Short term CGM trial for 1-2 weeks is a common practice among endocrinologists in the following situations: • In patients who has frequent hypoglycemia episodes • In patients with discrepancy between A1c and Self monitored blood glucose data • Uncontrolled diabetes

#	Indications	Rationale-CI
	individuals with type 2 diabetes	• To monitor the trends of hyperglycemia and hypoglycemia to guide insulin dosing decisions. • To screen for occult hypoglycemia episodes in patients with hypoglycemic awareness. • Preoperative optimization of glucose control before surgery • Post-operative optimization of glucose control after surgery • During pregnancy and to optimize glucose levels in the preconception period
2	Use of short-term (intermittent) glucose monitoring for individuals with type 2 diabetes	Based on the available evidence, endocrine society guidelines recommend short-term, intermittent RT-CGM use in adult patients with T2DM (not on prandial insulin) who have A1C levels ≥7% and are willing and able to use the device. I agree with this recommendation. • Peters AL, Ahmann AJ, Battelino T, et al. Diabetes Technology—Continuous Subcutaneous Insulin Infusion Therapy and Continuous Glucose Monitoring in Adults: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab. 2016 101(11):3922-3937. PMID: 27588440
3	Use of short-term (intermittent) glucose monitoring for individuals with type 2 diabetes	Data is very limited for the use of short-term (intermittent) glucose monitoring in persons with T2DM. Devices designed for short-term use are generally used for diagnostic purposes and are blinded to the patient. The downloaded data is used by clinicians to highlight problems and refine treatment. These diagnostic, or professional devices, are available, but are not suited for intermittent use, since either the patient or the device has to be returned to the center for download, and information is generally not available in real time. Current devices are better suited for continuous use, and involve the patient using a phone or dedicated reader to access glucose information. Experience with self-monitoring of blood glucose (SMBG) and with CGM in T1DM suggests that other than diagnostic use, CGM or other monitoring should be an integral part of diabetes care and ongoing.

NR = not reported

2. Based on the evidence and your clinical experience for each of the use of **short-term (intermittent)** glucose monitoring for individuals with **type 1 diabetes** with the defined patient selection criteria described below:
    - Respond YES or NO for each clinical indication whether the intervention would be expected to provide a clinically meaningful improvement in net health outcome; AND
    - Rate your level of confidence in your YES or NO response using the 1 to 5 scale outlined below.

#	Indications	YES / NO	Low Confidence *1*	*2*	Intermediate Confidence *3*	*4*	High Confidence *5*
1	Use of short-term (intermittent) glucose monitoring for individuals with type 1 diabetes which is poorly controlled[1], despite current use of best practices and who are willing and able to use the device.	Yes				X	
	Use of short-term (intermittent) glucose monitoring for individuals with type 1 diabetes prior to insulin pump initiation to determine basal insulin levels and who are willing and able to use the device.	Yes				X	
2	Use of short-term (intermittent) glucose monitoring for individuals with type 1 diabetes which is poorly controlled[1], despite current use of best practices and who are willing and able to use the device.	Yes	X				
	Use of short-term (intermittent) glucose monitoring for individuals with type 1 diabetes prior to insulin pump initiation to determine basal insulin levels and who are willing and able to use the device.	Yes			X		
3	Use of short-term (intermittent) glucose monitoring for individuals with type 1 diabetes which is poorly	No			X		

#	Indications	YES / NO	Low Confidence 1	2	Intermediate Confidence 3	4	High Confidence 5
	controlled[1], despite current use of best practices and who are willing and able to use the device.						
	Use of short-term (intermittent) glucose monitoring for individuals with type 1 diabetes prior to insulin pump initiation to determine basal insulin levels and who are willing and able to use the device.	NR					

NR = not reported

3. Based on the evidence and your clinical experience for each of the use of **short-term (intermittent)** glucose monitoring for individuals with **type 1 diabetes** with the defined patient selection criteria described below:
   - Respond YES or NO for each clinical indication whether this intervention is consistent with generally accepted medical practice; AND
   - Rate your level of confidence in your YES or NO response using the 1 to 5 scale outlined below.

#	Indications	YES / NO	Low Confidence 1	2	Intermediate Confidence 3	4	High Confidence 5
1	Use of short-term (intermittent) glucose monitoring for individuals with type 1 diabetes which is poorly controlled[1], despite current use of best practices and who are willing and able to use the device.	Yes					X
	Use of short-term (intermittent) glucose monitoring for individuals with type 1 diabetes prior to insulin pump initiation to determine basal insulin levels and who are willing and able to use the device.	Yes					X
2	Use of short-term (intermittent) glucose monitoring for individuals with type 1 diabetes which is poorly controlled[1], despite current use of best practices and who are willing and able to use the device.	Yes	X				
	Use of short-term (intermittent) glucose monitoring for individuals with type 1 diabetes prior to insulin pump initiation to determine basal insulin levels and who are willing and able to use the device.	Yes		X			
3	Use of short-term (intermittent) glucose monitoring for individuals with type 1 diabetes which is poorly controlled[1], despite current use of best practices and who are willing and able to use the device.	NR					
	Use of short-term (intermittent) glucose monitoring for individuals with type 1 diabetes prior to insulin pump initiation to determine basal insulin levels and who are willing and able to use the device.	NR					

NR = not reported

4. Based on the evidence and your clinical experience for each of the use of **long-term (continuous)** glucose monitoring for individuals with **type 2 diabetes** with the defined patient selection criteria described below:

- Respond YES or NO for each clinical indication whether the intervention would be expected to provide a clinically meaningful improvement in net health outcome; AND
- Rate your level of confidence in your YES or NO response using the 1 to 5 scale outlined below.

#	Indications	YES / NO	Low Confidence *1*	*2*	Intermediate Confidence *3*	*4*	High Confidence *5*
1	Use of long-term (continuous) glucose monitoring for individuals with type 2 diabetes who are insulinopenic and require multiple daily injections of insulin but who are poorly controlled[2]despite use of best practices and who are willing and able to use the device.	Yes				X	
2	Use of long-term (continuous) glucose monitoring for individuals with type 2 diabetes who are insulinopenic and require multiple daily injections of insulin but who are poorly controlled[2] despite use of best practices and who are willing and able to use the device.	Yes				X	
3	Use of long-term (continuous) glucose monitoring for individuals with type 2 diabetes who are insulinopenic and require multiple daily injections of insulin but who are poorly controlled[2] despite use of best practices and who are willing and able to use the device.	Yes					X

NR = not reported

5. Based on the evidence and your clinical experience for each of the use of **long-term (continuous)** glucose monitoring for individuals with **type 2 diabetes** with the defined patient selection criteria described below:
   - Respond YES or NO for each clinical indication whether this intervention is consistent with generally accepted medical practice; AND
   - Rate your level of confidence in your YES or NO response using the 1 to 5 scale outlined below.

#	Indications	YES / NO	Low Confidence *1*	*2*	Intermediate Confidence *3*	*4*	High Confidence *5*
1	Use of long-term (continuous) glucose monitoring for individuals with type 2 diabetes who are insulinopenic and require multiple daily injections of insulin but who are poorly controlled[2] despite use of best practices and who are willing and able to use the device.	Yes					X
2	Use of long-term (continuous) glucose monitoring for individuals with type 2 diabetes who are insulinopenic and require multiple daily injections of insulin but who are poorly controlled[2] despite use of best practices and who are willing and able to use the device.	Yes				X	
3	Use of long-term (continuous) glucose monitoring for individuals with type 2 diabetes who are insulinopenic and require multiple daily injections of insulin but who are poorly controlled[2] despite use of best practices and who are willing and able to use the device.	NR					

NR = not reported

6. Based on the evidence and your clinical experience for each of the use of **short-term (intermittent)** glucose monitoring for individuals with **type 2 diabetes** with the defined patient selection criteria described below:
   - Respond YES or NO for each clinical indication whether the intervention would be expected to provide a clinically meaningful improvement in net health outcome; AND
   - Rate your level of confidence in your YES or NO response using the 1 to 5 scale outlined below.

#	Indications	YES / NO	Low Confidence *1*	*2*	Intermediate Confidence *3*	*4*	High Confidence *5*
1	Use of short-term (intermittent) glucose monitoring for individuals with type 2 diabetes who are insulinopenic and require multiple daily injections of insulin but who are poorly controlled[2]despite use of best practices and who are willing and able to use the device.	Yes				X	
	Use of short-term (intermittent) glucose monitoring for individuals with type 2 diabetes who are insulinopenic and require multiple daily injections of insulin prior to insulin pump initiation to determine basal insulin levels and who are willing and able to use the device.	Yes				X	
2	Use of short-term (intermittent) glucose monitoring for individuals with type 2 diabetes who are insulinopenic and require multiple daily injections of insulin but who are poorly controlled[2]despite use of best practices and who are willing and able to use the device.	Yes					X
	Use of short-term (intermittent) glucose monitoring for individuals with type 2 diabetes who are insulinopenic and require multiple daily injections of insulin prior to insulin pump initiation to determine basal insulin levels and who are willing and able to use the device.	Yes					X
3	Use of short-term (intermittent) glucose monitoring for individuals with type 2 diabetes who are insulinopenic and require multiple daily injections of insulin but who are poorly controlled[2]despite use of best practices and who are willing and able to use the device.	No			X		
	Use of short-term (intermittent) glucose monitoring for individuals with type 2 diabetes who are insulinopenic and require multiple daily injections of insulin prior to insulin pump initiation to determine basal insulin levels and who are willing and able to use the device.	NR					

NR = not reported

7. Based on the evidence and your clinical experience for each of the use of **short-term (intermittent)** glucose monitoring for individuals with **type 2 diabetes** with the defined patient selection criteria described below:
   - Respond YES or NO for each clinical indication whether this intervention is consistent with generally accepted medical practice; AND
   - Rate your level of confidence in your YES or NO response using the 1 to 5 scale outlined below.

#	Indications	YES / NO	Low Confidence		Intermediate Confidence		High Confidence
			1	*2*	*3*	*4*	*5*
1	Use of short-term (intermittent) glucose monitoring for individuals with type 2 diabetes who are insulinopenic and require multiple daily injections of insulin but who are poorly controlled[2] despite use of best practices and who are willing and able to use the device.	Yes				X	
	Use of short-term (intermittent) glucose monitoring for individuals with type 2 diabetes who are insulinopenic and require multiple daily injections of insulin prior to insulin pump initiation to determine basal insulin levels and who are willing and able to use the device.	Yes				X	
2	Use of short-term (intermittent) glucose monitoring for individuals with type 2 diabetes who are insulinopenic and require multiple daily injections of insulin but who are poorly controlled[2] despite use of best practices and who are willing and able to use the device.	Yes					X
	Use of short-term (intermittent) glucose monitoring for individuals with type 2 diabetes who are insulinopenic and require multiple daily injections of insulin prior to insulin pump initiation to determine basal insulin levels and who are willing and able to use the device.	Yes					X
3	Use of short-term (intermittent) glucose monitoring for individuals with type 2 diabetes who are insulinopenic and require multiple daily injections of insulin but who are poorly controlled[2] despite use of best practices and who are willing and able to use the device.						
	Use of short-term (intermittent) glucose monitoring for individuals with type 2 diabetes who are insulinopenic and require multiple daily injections of insulin prior to insulin pump initiation to determine basal insulin levels and who are willing and able to use the device.						

NR = not reported

8. Additional narrative rationale or comments regarding the clinical context or specific clinical pathways for this topic and/or any relevant scientific citations (including the PMID) with evidence that demonstrates health outcomes you would like to highlight.

#	Additional Comments
1	1. Hypoglycemia is a limiting factor for aggressive insulin dose adjustments, robust real time data offered by CGM will helps guide physicians to adjust the insulin regimen accurately and and will aid patients to comply with the recommended regimen appropriately, as patients are reassured by the continuous surveillance from CGM. 2. Limitations of using A1c as an outcome measure: • HbA1c reflects average measurements- and may mask large variations in glycemic control • A1c does not address hypoglycemia and which is associated with adverse outcomes. • Different glycation potentials cause variation in the A1c levels for the same glucose levels. Increasingly it is being recognized A1c by itself is not the end outcome measure and alternative metrics like glucose time in range and glycemic variability should be used. CGM plays an important role in evaluating these metrics

#	Additional Comments
	• Sagar R, Abbas A, Ajjan R. Glucose monitoring in diabetes: from clinical studies to real-world practice. Practical Diabetes. March 2019 accessible at URL: https://www.practicaldiabetes.com/article/glucose-monitoring-in-diabetes-from-clinical-studies-to-real-world-practice/ 3. CGMS offers a practical way for diabetes patient to comply with glucose check monitoring recommendations and decreases the disease burden of the patients and improving patient quality of life both by making glucose testing easier and painless 4. Due to the above reasons CGM should be offered as an option for all patients with Type1 and Type2 diabetes patients on intensive insulin treatment. • Mancini G, Berioli MG, Santi E, et al. Flash Glucose Monitoring: A Review of the Literature with a Special Focus on Type 1 Diabetes. Nutrients. 2018 Aug;10(8):992. PMID: 30060632 • Sagar R, Abbas A, Ajjan R. Glucose monitoring in diabetes: from clinical studies to real-world practice. Practical Diabetes. March 2019 accessible at URL: https://www.practicaldiabetes.com/article/glucose-monitoring-in-diabetes-from-clinical-studies-to-real-world-practice/
2	Not applicable
3	Two facts are indisputable: first that hyperglycemia over time causes microvascular complications that can shorten the quantity and quality of life; and second that persons who take exogenous insulin are at risk for hypoglycemic events. Glucose monitoring plays an important role in reducing both of these risks. Continuous glucose monitoring has been shown to increase "time in range" (generally glucoses of 70 - 180 mg/dl) and reduce time spent in hypoglycemia. There is no question that persons with T1DM should have access to CGM, despite their current HbA1c. Patients with T2DM who are insulin-treated should also have access to continuous CGM for safety and to help achieve glycemic goals. Given the lower glucose targets in pregnancy, any woman who requires insulin during pregnancy, whether T1DM, T2DM or gestational diabetes, should also have access to CGM. Patients with T2DM who are not at risk for hypoglycemia and who currently do SMBG infrequently may find that the increased information provided by continuous use of CGM helps with lifestyle choices and modifications in a cost-effective way, however it is not needed for safety. Children and others who require insulin or who are otherwise at risk for hypoglycemia, and who have a responsible caretaker, should have access to CGM with a data-share feature so that the responsible caretaker can monitor glucose levels. Current CGM systems are not substantially more difficult to use than SMBG, however diabetes education or instruction in device use should be available to those not familiar with the technology.

NR = not reported

9. Is there any evidence missing from the attached draft review of evidence that demonstrates clinically meaningful improvement in net health outcome? If YES, please share any relevant scientific citations of missing evidence (including the PMID).

#	YES / NO	Citations of Missing Evidence
1	Yes	• Anjana RM, Kesavadev J, Neeta D, et al. A Multicenter Real-Life Study on the Effect of Flash Glucose Monitoring on Glycemic Control in Patients with Type 1 and Type 2 Diabetes. Diabetes Technol Ther. 2017 Sep;19(9):533-540. PMID: 28930495 • Landau Z, Abiri S, Gruber N et al. Use of flash glucose-sensing technology (FreeStyle Libre) in youth with type 1 diabetes: AWeSoMe study group real-life observational experience. Acta Diabetol. 2018 Dec;55(12):1303-1310. PMID: 30171412 • Yaron M, Roitman E, Aharon-Hananel G, et al. Effect of Flash Glucose Monitoring Technology on Glycemic Control and Treatment Satisfaction in Patients With Type 2 Diabetes. Diabetes Care. 2019; pii:dc180166. [Epub ahead of print] PMID 31036546 • Dunn TC, Xu Y, Hayter G et al. Real-world flash glucose monitoring patterns and associations between self-monitoring frequency and glycaemic measures: A European analysis of over 60 million glucose tests. Diabetes Res Clin Pract. 2018 Mar;137:37-46. PMID 29278709 • Haak T, Hanaire H, Ajjan R et al. Flash Glucose-Sensing Technology as a Replacement for Blood Glucose Monitoring for the Management of Insulin-Treated Type 2 Diabetes: a

#	YES / NO	Citations of Missing Evidence
		Multicenter, Open-Label Randomized Controlled Trial. Diabetes Ther (2017 Feb) 8(1):55-73. PMID: 28000140
2	No	Not applicable
3	Yes	Additional information to consider: CGM has been shown to improve neonatal outcomes in women with T1DM, reducing the incidence of large for gestational age (odds ratio 0.51, 95% CI 0.28 – 0.90, p=0.021); fewer neonatal intensive care admissions lasting more than 24 hours (odds ratio 0.48; 0.26 – 0.86; p=0.00157); and 1-day shorter length of hospital stay (p=0.0091). • Feig DS, Donovan LE, Corcoy R, et al. Continuous glucose monitoring in pregnant women with type 1 diabetes (CONCEPTT): a multicentre international randomised controlled trial. Lancet. 2017;390(10110):2347-2359. PMID: 28923465 Continuous CGM use has been shown to reduce health care utilization in persons with T1DM. • Parkin CG, Graham C, Smolskis J. Continuous Glucose Monitoring Use in Type 1 Diabetes: Longitudinal Analysis Demonstrates Meaningful Improvements in HbA1c and Reductions in Health Care Utilization. J Diabetes Sci Technol. 2017;11(3):522-528. PMID: 28745091 A meta-analysis of real-time and retrospective (intermittent) CGM use showed reduced HbA1c in persons with T2DM. • Ida S, Kaneko R, Murata K. Utility of Real-Time and Retrospective Continuous Glucose Monitoring in Patients with Type 2 Diabetes Mellitus: A Meta-Analysis of Randomized Controlled Trials. J Diabetes Res. 2019 Jan;15;2019:4684815. PMID: 30775385 Baseline glycated hemoglobin values predict the magnitude of improvement in patients with both T1DM and T2DM, with greater A1c drops in persons with higher A1c. • Billings LK, Parkin CG, Price D. Baseline Glycated Hemoglobin Values Predict the Magnitude of Glycemic Improvement in Patients with Type 1 and Type 2 Diabetes: Subgroup Analyses from the DIAMOND Study Program. Diabetes Technol Ther. 2018;20(8):561-565. PMID: 30044123

[1] Type 1 diabetes which is poorly controlled includes the following clinical situations: unexplained hypoglycemic episodes, hypoglycemic unawareness, suspected postprandial hyperglycemia, and recurrent diabetic ketoacidosis.
[2] Type 2 diabetes which is poorly controlled includes the following clinical situations: unexplained hypoglycemic episodes, hypoglycemic unawareness, and persistent hyperglycemia and A1C levels above target.

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Documentation for Clinical Review

Please provide the following documentation:

Initial Request:

- History and physical and/or consultation notes from referring physician including:
  - Type of diabetes and duration, reason for the request
  - Provider attestation that the patient has insulin dependent (type 1 or type 2) diabetes requiring multiple daily doses of insulin
  - Current insulin therapy and recent adjustments
  - Reason for short term need if appropriate
- Documented frequency of glucose self-testing and number of insulin injections per day or self-adjustments on an insulin pump (i.e., blood sugar and insulin logs), for the past 30 days to support the provider attestation
- Type (name) of device being requested

Replacements and/or Repair:

- Clinical summary including:
  - Type of diabetes and insulin management
  - Past benefit from CGM device, including clinical findings
  - Reason for continued need of CGM device
  - Description of device malfunction
- Warranty information and repair log or repair history (if applicable)

Post Service (in addition to the above, please include the following):

- All requirements for an initial request, plus:
  - Results/reports of blood sugar and insulin logs performed or device report of data

Coding

This Policy relates only to the services or supplies described herein. Benefits may vary according to product design; therefore, contract language should be reviewed before applying the terms of the Policy.

The following codes are included below for informational purposes. Inclusion or exclusion of a code(s) does not constitute or imply member coverage or provider reimbursement policy. Policy Statements are intended to provide member coverage information and may include the use of some codes for clarity. The Policy Guidelines section may also provide additional information for how to interpret the Policy Statements and to provide coding guidance in some cases.

Type	Code	Description
CPT®	95249	Ambulatory continuous glucose monitoring of interstitial tissue fluid via a subcutaneous sensor for a minimum of 72 hours; patient-provided equipment, sensor placement, hook-up, calibration of monitor, patient training, and printout of recording
	95250	Ambulatory continuous glucose monitoring of interstitial tissue fluid via a subcutaneous sensor for a minimum of 72 hours; physician or other qualified health care professional (office) provided equipment, sensor placement, hook-up, calibration of monitor, patient training, removal of sensor, and printout of recording
	95251	Ambulatory continuous glucose monitoring of interstitial tissue fluid via a subcutaneous sensor for a minimum of 72 hours; analysis, interpretation and report
	99091	Collection and interpretation of physiologic data (e.g., ECG, blood pressure, glucose monitoring) digitally stored and/or transmitted by the patient and/or caregiver to the physician or other qualified health care professional, qualified by education, training, licensure/regulation (when applicable) requiring a minimum of 30 minutes of time, each 30 days
	0446T	Creation of subcutaneous pocket with insertion of implantable interstitial glucose sensor, including system activation and patient training
	0447T	Removal of implantable interstitial glucose sensor from subcutaneous pocket via incision
	0448T	Removal of implantable interstitial glucose sensor with creation of subcutaneous pocket at different anatomic site and insertion of new implantable sensor, including system activation
HCPCS	A4226	Supplies for maintenance of insulin infusion pump with dosage rate adjustment using therapeutic continuous glucose sensing, per week
	A4238	Supply allowance for adjunctive, nonimplanted continuous glucose monitor (CGM), includes all supplies and accessories, 1 month supply = 1 unit of service ***(Code revision effective 1/1/2023)***
	A4239	Supply allowance for nonadjunctive, nonimplanted continuous glucose monitor (CGM), includes all supplies and accessories, 1 month supply = 1 unit of service ***(Code effective 1/1/2023)***
	A9276	Sensor; invasive (e.g., subcutaneous), disposable, for use with nondurable medical equipment interstitial continuous glucose monitoring system (CGM), one unit = 1 day supply ***(Code effective 1/1/2023)***
	A9277	Transmitter; external, for use with nondurable medical equipment interstitial continuous glucose monitoring system (CGM) ***(Code effective 1/1/2023)***

Type	Code	Description
	A9278	Receiver (monitor); external, for use with nondurable medical equipment interstitial continuous glucose monitoring system (CGM) ***(Code effective 1/1/2023)***
	E0787	External ambulatory infusion pump, insulin, dosage rate adjustment using therapeutic continuous glucose sensing
	E2102	Adjunctive, nonimplanted continuous glucose monitor (CGM) or receiver ***(Code revision effective 1/1/2023)***
	E2103	Nonadjunctive, nonimplanted continuous glucose monitor (CGM) or receiver ***(Code effective 1/1/2023)***
	G0308	Creation of subcutaneous pocket with insertion of 180 day implantable interstitial glucose sensor, including system activation and patient training ***(Deleted code effective 1/1/2023)***
	G0309	Removal of implantable interstitial glucose sensor with creation of subcutaneous pocket at different anatomic site and insertion of new 180 day implantable sensor, including system activation ***(Deleted code effective 1/1/2023)***
	K0553	Supply allowance for therapeutic continuous glucose monitor (CGM), includes all supplies and accessories, 1 month supply = 1 unit of service ***(Deleted code effective 1/1/2023)***
	K0554	Receiver (monitor), dedicated, for use with therapeutic glucose continuous monitor system ***(Deleted code effective 1/1/2023)***
	S1030	Continuous noninvasive glucose monitoring device, purchase (for physician interpretation of data, use CPT code)
	S1031	Continuous noninvasive glucose monitoring device, rental, including sensor, sensor replacement, and download to monitor (for physician interpretation of data, use CPT code)

Policy History

This section provides a chronological history of the activities, updates and changes that have occurred with this Medical Policy.

Effective Date	Action
03/01/2020	New policy. Coding Update.
02/01/2021	Annual review. Policy statement, guidelines and literature updated.
02/01/2022	Annual review. Policy statement, guidelines and literature updated. Policy title changed from Continuous or Intermittent Monitoring of Glucose in the Interstitial Fluid to current one.
06/01/2022	Annual review. Policy statement and guidelines updated. Coding Update.
09/01/2022	Annual review. Policy statement, guidelines and literature updated. Coding update.
04/01/2023	Annual review. Policy statement and guidelines updated. Coding update.
09/01/2023	Administrative update. No change to policy statement. Literature review updated. Coding Update.

Definitions of Decision Determinations

Medically Necessary: Services that are Medically Necessary include only those which have been established as safe and effective, are furnished under generally accepted professional standards to treat illness, injury or medical condition, and which, as determined by Blue Shield, are: (a) consistent with Blue Shield medical policy; (b) consistent with the symptoms or diagnosis; (c) not furnished

primarily for the convenience of the patient, the attending Physician or other provider; (d) furnished at the most appropriate level which can be provided safely and effectively to the patient; and (e) not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of the Member's illness, injury, or disease.

Investigational/Experimental: A treatment, procedure, or drug is investigational when it has not been recognized as safe and effective for use in treating the particular condition in accordance with generally accepted professional medical standards. This includes services where approval by the federal or state governmental is required prior to use, but has not yet been granted.

Split Evaluation: Blue Shield of California/Blue Shield of California Life & Health Insurance Company (Blue Shield) policy review can result in a split evaluation, where a treatment, procedure, or drug will be considered to be investigational for certain indications or conditions, but will be deemed safe and effective for other indications or conditions, and therefore potentially medically necessary in those instances.

Prior Authorization Requirements and Feedback (as applicable to your plan)

Within five days before the actual date of service, the provider must confirm with Blue Shield that the member's health plan coverage is still in effect. Blue Shield reserves the right to revoke an authorization prior to services being rendered based on cancellation of the member's eligibility. Final determination of benefits will be made after review of the claim for limitations or exclusions.

Questions regarding the applicability of this policy should be directed to the Prior Authorization Department at (800) 541-6652, or the Transplant Case Management Department at (800) 637-2066 ext. 3507708 or visit the provider portal at www.blueshieldca.com/provider.

We are interested in receiving feedback relative to developing, adopting, and reviewing criteria for medical policy. Any licensed practitioner who is contracted with Blue Shield of California or Blue Shield of California Promise Health Plan is welcome to provide comments, suggestions, or concerns. Our internal policy committees will receive and take your comments into consideration.

For utilization and medical policy feedback, please send comments to: MedPolicy@blueshieldca.com

Disclaimer: This medical policy is a guide in evaluating the medical necessity of a particular service or treatment. Blue Shield of California may consider published peer-reviewed scientific literature, national guidelines, and local standards of practice in developing its medical policy. Federal and state law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over medical policy and must be considered first in determining covered services. Member contracts may differ in their benefits. Blue Shield reserves the right to review and update policies as appropriate.

Appendix A

POLICY STATEMENT (No changes)	
BEFORE	**AFTER**
Continuous Glucose Monitoring 1.01.20 **Policy Statement:** I. Continuous glucose monitoring (CGM) of glucose levels in interstitial fluid, as a technique of diabetic monitoring, may be considered **medically necessary** when **both** of the following situations occur: A. Individuals with insulin dependent (type 1 or type 2) diabetes requiring multiple (three or more) daily doses of insulin B. The device includes an audible or tactile (vibrating) alarm for low glucose alerts without patient intervention (NOTE: the FreeStyle Libre 14 day device does not have alarms but the FreeStyle Libre 2 does have appropriate alarms, as do Dexcom G5 and G6) II. The use of implantable CGM devices (e.g., Eversense®) for management of Type 1 and Type 2 diabetes mellitus is considered **investigational** (see Policy Guidelines section). III. The use of continuous noninvasive glucose monitoring devices (see Policy Guidelines section) are considered **investigational.** IV. Other uses of long-term CGM of glucose levels as a technique of diabetic monitoring in individuals who are not insulin dependent (including use in gestational diabetes) are considered **investigational**.	**Continuous Glucose Monitoring 1.01.20** **Policy Statement:** I. Continuous glucose monitoring (CGM) of glucose levels in interstitial fluid, as a technique of diabetic monitoring, may be considered **medically necessary** when **both** of the following situations occur: A. Individuals with insulin dependent (type 1 or type 2) diabetes requiring multiple (three or more) daily doses of insulin B. The device includes an audible or tactile (vibrating) alarm for low glucose alerts without patient intervention (NOTE: the FreeStyle Libre 14 day device does not have alarms but the FreeStyle Libre 2 does have appropriate alarms, as do Dexcom G5 and G6) II. The use of implantable CGM devices (e.g., Eversense®) for management of Type 1 and Type 2 diabetes mellitus is considered **investigational** (see Policy Guidelines section). III. The use of continuous noninvasive glucose monitoring devices (see Policy Guidelines section) are considered **investigational.** IV. Other uses of long-term CGM of glucose levels as a technique of diabetic monitoring in individuals who are not insulin dependent (including use in gestational diabetes) are considered **investigational**.