

HEALTH EVIDENCE REVIEW COMMISSION (HERC)

COVERAGE GUIDANCE: CONTINUOUS GLUCOSE MONITORING IN DIABETES MELLITUS

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HERC COVERAGE GUIDANCE

Continuous blood glucose monitoring with real-time or retrospective continuous glucose monitoring systems should only be covered for Type 1 diabetes mellitus patients for whom insulin pump management is being considered, initiated, or utilized and who also have one of the following:

- HbA1c levels greater than 8.0% despite compliance with therapy, or
- a history of recurrent hypoglycemia.

Real-time and retrospective continuous glucose monitoring systems should not be covered for Type 2 diabetes mellitus patients.

RATIONALE FOR GUIDANCE DEVELOPMENT

The HERC selects topics for guideline development or technology assessment based on the following principles:

- Represents a significant burden of disease
- Represents important uncertainty with regard to efficacy or harms
- Represents important variation or controversy in clinical care
- Represents high costs, significant economic impact
- Topic is of high public interest

Coverage guidance development follows to translate the evidence review to a policy decision. Coverage guidance may be based on an evidence-based guideline developed by the Evidence-based Guideline Subcommittee or a health technology assessment developed by the Health Technology Assessment Subcommittee. In addition, coverage guidance may utilize an existing evidence report produced by one of HERC's trusted sources, generally within the last three years.

EVIDENCE SOURCES

Langendam M, Luijf YM, Hooft L, DeVries JH, Mudde AH, Scholten RJPM. (2012). Continuous glucose monitoring systems for type 1 diabetes mellitus. *Cochrane Database of Systematic Reviews*, Issue 1. Art. No.: CD008101. DOI: 10.1002/14651858.CD008101.pub2. Retrieved from <http://summaries.cochrane.org/CD008101/continuous-glucose-monitoring-systems-for-type-1-diabetes-mellitus>

Golden, S.H., Brown, T., Yeh, H.C., Maruthur, N., Ranasinghe, P., Berger, Z., et al. (2012). Methods for Insulin Delivery and Glucose Monitoring: Comparative Effectiveness. Comparative Effectiveness Review No. 57. (Prepared by Johns Hopkins University Evidence-based Practice Center under Contract No. 290-2007-10061-I.) AHRQ Publication No. 12-EHC036-EF. Rockville, MD: Agency for Healthcare Research and Quality. Retrieved from www.effectivehealthcare.ahrq.gov/reports/final.cfm

The summary of evidence in this document is derived directly from these evidence sources, and portions are extracted verbatim.

SUMMARY OF EVIDENCE

Clinical Background

Diabetes mellitus (DM) is a metabolic disorder resulting from a defect in insulin secretion, insulin action, or both. A consequence of this is chronic hyperglycemia with disturbances of carbohydrate, fat and protein metabolism. Long-term complications of DM include retinopathy, nephropathy and neuropathy, and the risk of cardiovascular disease is increased. There are several types of diabetes. In type 1 DM the body is unable to produce insulin and therefore people with this type are treated with insulin. Type 1 DM accounts for 10% of cases, is typically seen at onset in children and young adults (less than 30 years), and is often referred to as insulin dependent diabetes.

Self-monitoring of blood glucose (SMBG) is an essential part of diabetes management and is used to optimize glycemic control. Regular testing of blood glucose levels allows patients with diabetes to adjust insulin dosage appropriately, and is typically done using a finger capillary blood sample and a blood glucose meter several times per day. Continuous glucose monitoring (CGM) systems measure interstitial fluid glucose levels to provide semi-continuous information about glucose levels, which may identify fluctuations that would not be identified with self-monitoring alone. Continuous glucose monitoring is considered to be particularly useful for children (to reduce the often very high number of finger punctures in this group), for patients with poorly controlled diabetes, for pregnant women in whom tight glucose control is essential with respect to the outcome of pregnancy and for patients with hypoglycemia unawareness (to prevent dangerous episodes of hypoglycemia). There are two types of CGM systems:

- those that measure the glucose concentration during a certain time span, storing the information in a monitor that can be downloaded later

- real-time systems that continuously provide the actual glucose concentration on a display.

Continuous glucose monitoring can be used continuously or intermittently (e.g., a couple of days per month or in intervals of three days). Evaluation of blood sugar control is generally done by monitoring changes in HbA1c. A clinically significant change in this value is generally considered to be 0.5%.

Evidence Review

Cochrane Review

Children

Four out of the five randomized controlled trials (RCT) that evaluated retrospective CGM systems found that HbA1c levels decreased in both the CGM and SMBG group during follow-up, while one found that HbA1c level did not change in the CGM group but decreased in the SMBG group. The mean difference between the CGM group and the SMBG group in change in HbA1c ranged from -0.5% to 0.1%, but was not statistically significant in any of the five RCTs.

Severe hypoglycemia was measured in four studies. The occurrence of events was very low, and there were no significant differences between groups. Ketoacidosis was measured in one study, but again, the number of events was very small. The one RCT that measured quality of life found no significant differences between CGM and SMBG.

All three studies that evaluated real-time systems found that the HbA1c levels in both the CGM and SMBG group declined during the study period. Three months after baseline the difference in change was statistically significant in favor of CGM (change in HbA1c -0.5% versus -0.2%). At six months and 12 months follow-up, however, the difference in change in HbA1c level was no longer significant. Another outcome examined was the proportion of patients who improved their HbA1c level by at least 0.5%, which is generally considered a change that is clinically significant. When evaluating that outcome, the proportion of patients who improved their HbA1c level by at least 0.5% was significantly larger in the CGM group at three months and at six months after baseline. The occurrence of severe hypoglycemia after six months of follow-up was somewhat lower in the CGM study arm, but the difference was not statistically significant. Ketoacidosis events did not occur at six months follow-up and rarely after 12 months follow-up. The two studies that examined quality of life found small differences that were not statistically significant.

Adolescents

The two studies that included adolescents both used real-time CGM systems. In both studies the HbA1c levels in the CGM and SMBG group declined during the study, but the differences were not statistically significant, and by six months follow-up, the differences were even less. The proportion of patients that had improved their HbA1c level by at least 0.5% was equal in both groups. Severe hypoglycemic and ketoacidotic events were infrequent, and there were no significant differences between the groups.

The outcomes of quality of life, patient satisfaction, diabetes complications, CGM-derived glucose control, death and costs were not measured in any of the studies in adolescents.

Adults

Change in HbA1c level was measured in two RCTs addressing retrospective CGM, neither of which found a significant difference in change between the study arms. The one study that reported severe hypoglycemia found no difference between groups.

Five studies evaluated real-time CGM systems, and found that the change in decrease in HbA1c varied between -0.1% and -1.1%, with this change being statistically significant in three of them. The same pattern was seen six and 12 months after baseline, although the number of studies was fewer. In one study, sensor usage of more than 60% was associated with HbA1c reduction, and a larger proportion of patients improved their HbA1c by at least 0.5% in the CGM group. (Compliance with protocol is generally considered to be sensor usage at least 70% of the time. Compliance varies significantly among studies, with some studies of adolescents having sensor usage as low as 30%.) One study measured HbA1c levels after 18 months follow-up and found the overall difference between groups was insignificant. Four studies measured the occurrence of severe hypoglycemia. At three months, the number of events was very low, and at six and 12 months, the risk of severe hypoglycemia was increased for CGM users, but the difference was not statistically significant. The number of ketoacidosis events was very small.

Two studies measured quality of life after six months and found the differences between the CGM and SMBG group were small and not statistically significant. Two studies investigated patient satisfaction, one after three months and one after six months follow-up, although for both, patients in the CGM group were using an insulin pump, while the SMBG used multiple daily injections of insulin. Patients in the CGM group scored significantly higher on overall satisfaction. The outcomes of diabetes complications, death and costs were not measured in any of the studies in adults.

Pregnant women with diabetes type

The only study on pregnant women with diabetes did not present the data for type 1 and type 2 diabetes separately, so it is not presented here.

Subgroup analysis

There were no studies that included patients with hypoglycemia unawareness. For studies that were limited to patients with poorly controlled diabetes (HbA1c greater than 8.0%), three were for retrospective CGM systems and four for real-time CGM. For the retrospective CGM systems, the evidence for improved glycemic control is conflicting. Significantly lower, as well as significantly higher HbA1c levels for the CGM group at the end of the study were found, and a third RCT showed no effect at all. For real-time CGM systems, there is limited evidence for improved glycemic control, with a statistically and clinically significant effect in two of the four RCTs. These two had the largest mean differences in the change in HbA1c of all studies that measured this outcome (-1.12% and -0.6%).

Meta-analysis including all age groups

There was a statistically significant larger decline in HbA1c level for real-time CGM users starting insulin pump therapy compared to patients using multiple daily injections of insulin and SMBG (mean difference in HbA1c level change from baseline -0.7%). For patients where only the CGM was a new device, the average decline in HbA1c level was also statistically significantly larger for CGM users compared to the SMBG users. However, the decline was much smaller than in the group with the sensor-augmented insulin pump: the average difference change in HbA1c was 0.2%. There were no statistically significant differences in the risk of severe hypoglycemia or ketoacidosis.

[\[Evidence Source\]](#)

AHRQ Review

Evidence was identified evaluating the comparative effectiveness of real-time CGM versus SMBG in individuals with type 1 diabetes only. Compared with SMBG, real-time CGM achieved a lower HbA1c, with a mean between-group difference of -0.30 percent. Slightly greater reductions occurred where sensor compliance was 60 percent or greater (mean difference of -0.36 percent). There was no difference in the rate of severe hypoglycemia or quality of life. The evidence for other outcomes was low or insufficient. For CGM that is used in combination with an insulin pump, CGM achieved a greater reduction in HbA1c compared to multiple daily injections of insulin with SMBG, with a mean between-group difference of -0.68 percent. There was no difference in the rate of hypoglycemia, but the CGM group had significantly less hyperglycemia. There were no studies of the comparative effectiveness of real-time CGM versus SMBG in individuals with type 2 diabetes.

[\[Evidence Source\]](#)

Overall Summary

Retrospective CGMs are not more efficacious for any outcome, in any age group. There is some evidence that real-time CGM is more effective at decreasing HbA1c in children, although this does not appear to be the case for adolescents. In adults, there is also some evidence that real-time CGM is more effective at decreasing HbA1c, although not all studies were statistically significant. The study with the longest period of follow up (18 months) found no differences. In addition, the amount of decrease in HbA1c may not be clinically significant (less than 0.5%), with two exceptions: studies that compared CGM plus insulin pump to multiple daily injections of insulin plus SMBG, and studies of poorly controlled diabetics (HbA1c > 8.0%). Two studies found no differences in quality of life, while two found increased patient satisfaction in the insulin pump plus CGM group (compared to multiple daily injections of insulin plus SMBG). There is no evidence of a difference between CGM and SMBG in the incidence of hypoglycemia or ketoacidosis. There is no evidence that addresses the effect of CGM on diabetic complications, costs or mortality.

PROCEDURE

Continuous Glucose Monitoring

DIAGNOSES

Type 1 Diabetes Mellitus

APPLICABLE CODES

CODES	DESCRIPTION
ICD-9 Diagnosis Codes	
250.x1	Diabetes Mellitus, type 1, not stated as uncontrolled
250.x3	Diabetes Mellitus, type 1, uncontrolled
ICD-9 Volume 3 (Procedure Codes)	
None	
CPT Codes	
83036	Hemoglobin; glycosylated (A1C)
83037	Hemoglobin; glycosylated (A1C) by device cleared by FDA for home use
95250-1	Glucose monitoring by SQ device
97802- 97804	Medical nutrition therapy
98960-98962	Education and training for patient self-management by a qualified, nonphysician health care professional using a standardized curriculum, face-to-face, with the patient (could include caregiver/ family) each 30 minutes
99078	Physician educational services rendered to patients in a group setting (eg, prenatal, obesity, or diabetic instructions)
HCPCS Codes	
A4230-2	Insulin infusion pump supplies
A4233-6	Batteries for home blood glucose monitors
A4253	Blood Glucose test strips, box of 50
A4255	Platforms for home blood glucose monitor, 50/box
A4256	Calibrator solutions/chips
A4258	Spring-powered device for lancet, each
A4259	Lancets, per box of 100
A9274	External ambulatory insulin delivery system, disposable
A9276	Disposable sensor, CGM system
A9277	External transmitter, CGM system
A9278	External receiver, CGM system
E0607	Blood glucose monitor
E0784	Insulin infusion pump
E2100	Blood glucose monitor with voice synthesizer
E2101	Blood glucose monitor with integrated lancer
G0108-G0109	Diabetes outpatient self-management training services
G0270-G0271	Medical nutrition therapy; reassessment and subsequent intervention(s) following second referral in same year for change in diagnosis, medical condition or treatment regimen (including additional hours needed for renal disease)
S1030-1	Continuous non-invasive glucose monitoring device, purchase/rental
S9140	Diabetic management program, follow-up visit to non-MD provider
S9141	Diabetic management program, follow-up visit to MD provider

Note: Inclusion on this list does not guarantee coverage

Coverage guidance is prepared by the Health Evidence Review Commission (HERC), HERC staff, and subcommittee members. The evidence summary is prepared by the Center for Evidence-based Policy at Oregon Health & Science University (the Center). This document is intended to guide public and private purchasers in Oregon in making informed decisions about health care services.

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