FINAL key questions and background

Continuous glucose monitoring

Background

Diabetes mellitus (DM), or diabetes, is a serious metabolic disease characterized by chronic elevation of blood glucose (i.e., hyperglycemia) resulting from defects in insulin secretion, insulin action, or both. No definitive cure is known at this time. Diabetes is generally categorized into three major types based on etiology: Type 1 diabetes (T1DM) (formerly called juvenile diabetes or insulin-dependent diabetes mellitus [IDDM]), Type 2 diabetes (T2DM) (formerly called adult onset diabetes mellitus [AODM] or non-insulin dependent diabetes [NIDDM]), and gestational diabetes mellitus (GDM).

Diabetes is a leading cause of morbidity and mortality and is associated with substantial healthcare and societal costs. An estimated 29.9 million Americans (9.3% of the population) had diabetes in 2015 and, by 2050, the prevalence of diabetes in the U.S. adult population is projected to increase to between 21% and 33%. Serious complications related to diabetes include diabetic ketoacidosis (DKA) and hyperosmolar hyperglycemic nonketotic syndrome (HHNS), as well as longer term morbidity due to microvascular (e.g., retinopathy, nephropathy, neuropathy) and macrovascular (e.g., heart disease, stroke) complications; other diabetes related complications include increased risk of infections, cancer and other autoimmune disorders including celiac sprue, thyroid disease, rheumatoid arthritis, and vitiligo.

Intensive insulin therapy, a term used to describe tight management of blood glucose levels, has been shown to reduce the risk of long-term diabetic complications by lowering average blood sugar levels, but also increases the risk of hypoglycemia, which can result in serious morbidity and even death, and causes fear of hypoglycemia which is a major barrier to optimal glucose control.

Real-time continuous glucose monitoring (CGM) is advanced glucose monitoring technology that continuously measures interstitial glucose levels, displays the current blood glucose level as well as the direction and rate of change, and uses alarms and alerts to inform patients when blood glucose is exceeding or falling below specified thresholds. Conventional fingerstick self-monitoring of blood glucose (SMBG), sometimes called intermittent monitoring, is a technique for testing blood glucose using a portable glucose meter designed for home use. SMBG provides an instantaneous reading of current blood glucose levels at single points in time, but cannot indicate whether the glucose level is on its way up or down. CGMs were designed to aid in the detection of episodes of hyperglycemia and hypoglycemia, facilitating both acute and long term therapy adjustments, which may minimize these excursions. With the exception of one FDA-approved device (Dexcom G5 Mobile CGM System), CGMs are intended to complement, not replace, information obtained from a standard home glucose monitoring device; they are not intended to be used directly for making therapy adjustments, but rather to provide an indication of when a fingerstick may be required. CGMs can be used as stand-alone devices or in conjunction with compatible insulin pumps.

Policy context

This topic was originally reviewed in 2011. It is proposed for re-review based on new evidence and newly expanded indications for continuous glucose monitoring (CGM). New evidence and indications are identified that support re-reviewing the evidence for continuous glucose monitoring.

Objectives

The first aim of this report is to update the 2011 HTA on glucose monitoring in children and adolescents by systematically reviewing, critically appraising and analyzing new research evidence on the safety and efficacy of continuous glucose monitoring in persons under 18 years old with insulin requiring diabetes mellitus. The second aim is to systematically review, critically appraise and analyze research evidence on the safety and efficacy continuous glucose monitoring in persons with type 1 or type 2 diabetes (regardless of insulin requirement), including pregnant women with pre-existing or gestational diabetes. SMBG as a stand-alone means of monitoring blood glucose will not be included as an intervention.

Key questions

In persons with diabetes mellitus (DM):

1. What is the evidence of efficacy and effectiveness of continuous monitoring?
2. What is the evidence of the safety of continuous glucose monitoring?
3. What is the evidence that glucose monitoring has differential efficacy or safety issues in sub-populations?
4. What is the evidence of cost-effectiveness of continuous glucose monitoring?

Scope

Population: Persons with diabetes mellitus, including those with type 1 and type 2, and pregnant women with pre-existing diabetes or gestational diabetes

Interventions: FDA-approved real-time continuous glucose monitoring devices and FDA-approved combination devices integrating real-time continuous glucose monitoring with insulin pump/infusion (including sensor augmented insulin pumps).

Comparators: Self-monitoring using convention blood glucose meters, attention control, blinded/sham CGM, and usual care.

Outcomes:

Primary clinical outcomes:

- Microvascular complications (e.g., vision loss, kidney failure, peripheral neuropathy, objectively assessed)
- Macrovascular complications (e.g., coronary artery, cerebrovascular or peripheral arterial disease, objectively assessed)
- Fetal outcomes, cesarean section rates

Primary intermediate outcomes:

- Achieving target (i.e. age-appropriate) HgA1C level
- Maintaining target (i.e. age-appropriate) HgA1C level
- Acute episodes of hypoglycemia

Secondary intermediate outcomes

- Acute episodes of hyperglycemia
- Acute episodes of diabetic ketoacidosis
- Quality of life (validated instruments only)

Safety outcomes:

- Mortality
- Morbidity from glucose meters or monitors

Economic outcomes:

- Long term and short term comparative cost-effectiveness measures

Studies:

Only high quality (low risk of bias) comparative studies will be considered for Key Questions 1-3. Observational studies with longer term clinical outcomes or safety outcomes will be considered for Key Questions 1 and 3. Full, formal economic studies (i.e., cost-effectiveness, cost-utility, cost-minimization, and cost-benefit studies) will be sought for Key Question 4; studies using modeling may be used to determine cost-effectiveness over the full duration of glucose monitoring, which is a lifetime. Observational studies of safety will be considered.

Analytic framework
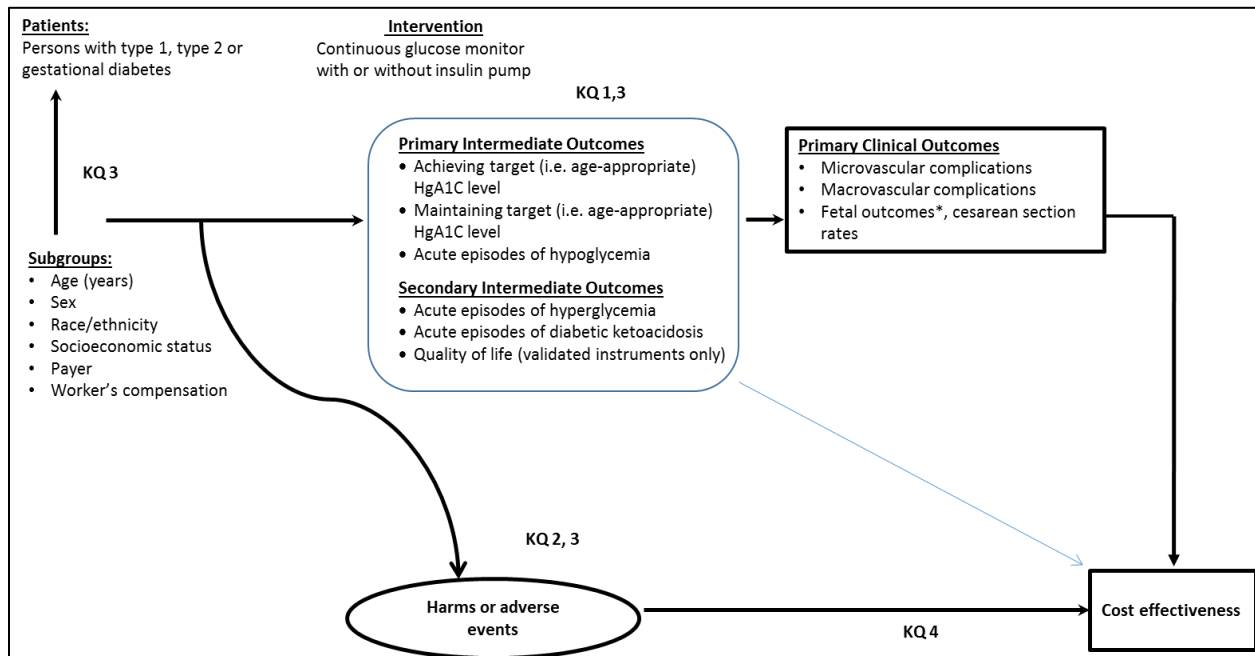
*Fetal outcomes include gestational age, birth weight, frequency of neonatal hypoglycemia, birth trauma, major and minor anomalies, admission to a neonatal intensive care unit, stillbirth, and neonatal and perinatal mortality.

Public comment and Response

See ***Draft key questions: Public comment and response*** document published separately.