MEDICARE COVERAGE ADVISORY COMMITTEE
GLUCOSE MONITORING
AUGUST 30, 2006

Evidence from clinical research has resulted in increasing consensus in several aspects of the monitoring and treatment of the young type 1 diabetic patient. Less evidence and consensus exists on the application of these principles to type 2 diabetic patients, particularly those in the older Medicare population. Newer technologies, such as continuous glucose monitoring and its potential application to an artificial pancreas, have a newer and less robust evidence base.

This MCAC will address these two major issues:
1. The current evidence on the role of the newer continuous glucose monitoring in type 1 diabetics and the type of research needed to clarify its role; and
2. The application of the principles of type 1 diabetes management to type 2 Medicare beneficiaries:
   - The role of outpatient glycemic control on the long-term clinical outcomes in type 2 diabetic patients $\geq$ 65 years of age;
   - The role of outpatient glucose monitoring on glycemic control and/or clinical outcomes in the Medicare population.

While of interest, this committee will not address the current evidence for monitoring Type 1 diabetes in Medicare beneficiaries outside the questions on continuous glucose monitoring.

In addition to evaluating the available data, the committee will identify areas in which the current data are deficient and in which additional research is warranted.

QUESTIONS

I. Outcomes

Question 1: How confident are you that macrovascular disease (fatal and non-fatal MI, stroke) is a more common cause of morbidity and mortality than microvascular disease (retinopathy resulting in legal blindness and renal disease resulting in dialysis) in Medicare patients with type 2 diabetes?

Very confident	Somewhat confident	Unsure	Somewhat unconfident	Very unconfident
5	4	3	2	1

Discussion Question:
- Do the kinds of chronic diabetes-associated complications that occur with type 2 diabetes differ qualitatively and quantitatively from those that occur with type 1 diabetes?

(Definition: Diabetic complications manifest by the following outcomes: cardiovascular events (MI, stroke), cardiovascular death, legal blindness, renal disease resulting in chronic dialysis, amputation, and all cause mortality.)

Question 2. Although the largest segments of the Medicare population are >65 and/or have type 2 diabetes, CMS is interested in the evidence base for newer technologies for glucose monitoring, including continuous monitoring of interstitial fluid and their role in type 1 diabetes. How confident are you that the effectiveness of continuous monitoring in patients with Type 1 diabetes is best assessed by changes in HbA1c, concomitant hypoglycemia rates, hypoglycemia-related falls, post-operative morbidity, wound-healing, and weight?

Very confident	Somewhat confident	Unsure	Somewhat unconfident	Very unconfident
5	4	3	2	1

Discussion Question:

- Should other outcomes be considered?
- Are there any chronic complications in type 1 patients ≥65 years of age that are substantively different from complications in type 1 patients <65 years of age and that would require special study?

II. Relationship of Glycemic Control (HbA1c) and Outcomes in Type 2 Diabetes

Question 3: There have been several large trials of glycemic control in relatively young patients (DCCT) and patients up to age 65 (UKPDS). How confident are you that glycemic control prevents or delays the onset of chronic complications, especially cardiovascular events and death, in patients who develop type 2 diabetes after age 64 and that the duration of complication delay, if any, is clinically, and not just statistically, significant. (Primary prevention)

Very confident	Somewhat confident	Unsure	Somewhat unconfident	Very unconfident
5	4	3	2	1

Question 4: How confident are you that glycemic control reverses or reduces progression of pre-existing chronic complications in a clinically meaningful way in patients who had type 2 diabetes prior to age 65? (Secondary prevention)

Very confident	Somewhat confident	Unsure	Somewhat unconfident	Very unconfident
5	4	3	2	1

Discussion Questions (regarding questions 3 and 4):

- Do changes in glycemic control result in similar reductions in the risk of developing different diabetic complications, such as foot ulcers, neuropathy, nephropathy?
- What change in HbA1c is needed to delay/reverse complications?
- Is the change in HbA1c needed to delay/reverse complications dependent on the absolute HbA1c value? In other words, is there a linear relationship between incremental changes in HbA1c and the delay or reversal of chronic complications in type 2 diabetes or is there an inflection point?
- Does age of diabetes onset affect any incremental benefit of glycemic control on chronic complications?

Question 5: The DCCT provided information on the frequency of clinically significant hypoglycemia (≤50 mg/dl and requiring third party intervention) in young type 1 patients and correlated hypoglycemic frequency with glycemic control. Because of the autoimmune nature of their disease, patients with type 1 disease do not have an endogenous insulin reserve that could modulate the effects of excess insulin doses and may lack glucagon for counter-regulatory response to hypoglycemia. These factors affect the frequency and severity of hypoglycemia.

Can the information on hypoglycemia in type 1 patients be generalized to Medicare-aged type 2 patients? More specifically, how confident are you that hypoglycemic risk (frequency and severity) for a given level of glycemic control is the same for patients with type 1 diabetes and type 2 diabetes?

(Definition: Hypoglycemia=Glucose <30 mg/dl and/or requiring third party intervention)

Very confident	Somewhat confident	Unsure	Somewhat unconfident	Very unconfident
5	4	3	2	1

Discussion Question:

- Does the frequency of hypoglycemia differ by the class of therapeutic agent (insulin, insulin secretagogue oral agent, non-insulin secretagogue oral agent, other parenteral agent), and/or target HbA1c level and/or insulin dose [e.g., ≥40 units/day versus <40 units/day]?
- In the DCCT, HbA1c was validated as a surrogate for young type 1 diabetic patients using insulin. Specific risk values for the development of hypoglycemia could be assigned to HbA1c values. Do these same risk values apply to the Medicare population with type 1 diabetes or the Medicare population with type 2 diabetes?
- Should the same HbA1c targets be employed for patients of all age groups, with different co-morbid conditions, and different histories of hypoglycemia? For example, should the target HbA1c for a 70-year-old patient with recurrent hypoglycemia be 7%?

III. Relationship between Glucose Monitoring and Glycemic Control (HbA1c)

Question 6: How confident are you that glucose monitoring improves, by a clinically meaningful degree, glycemic control (HbA1c) and decreases the risk for hypoglycemia at a given level of HbA1c?

Frequency monitoring	Type 1	Type 2 using diet or oral agents	Type 2 using insulin
Blood glucose >1x/day			
Blood glucose >2x/day			
Blood glucose >4x/day			
Continuous monitoring (interstitial fluid)			
Continuous monitoring + subcutaneous infusion pump			

Very confident	Somewhat confident	Unsure	Somewhat unconfident	Very unconfident
5	4	3	2	1

Discussion Questions:

- Does increased monitoring result in changes in medical management?
- Do the changes in medical management result in clinically significant improvements in glycemic control?
- Does age (<45, <55, <65, <75, ≥75) affect glycemia goals and frequency of monitoring?
- What is the frequency of monitoring required to reduce HbA1c by 1%?
- Is the frequency of monitoring required to lower HbA1c from 9% to 8% the same as the frequency of monitoring to lower HbA1c from 7.5% to 6.5%. In other words, is there an equivalent benefit of monitoring on glycemic control throughout the range of HbA1c values?
- Is the increased frequency of glucose monitoring alone, and not other concomitant patient variables, responsible for any improvement in glycemic control?
- How accurate are devices and does accuracy differ over the measurement range? How strong is the evidence that an improvement in device accuracy results in an improvement in (clinical or health) outcomes?
- What potential benefits does continuous glucose monitoring offer to Medicare-aged patients with diabetes, beyond simply more frequent glucose values?
- What are outstanding research questions are there for glucose monitoring, including continuous glucose monitoring?
- Do the issues of study design, study duration, and blinding impact interpretation of results of glucose monitoring studies?

IV. Relationship between Glucose Monitoring and Long-term Outcomes in Diabetes

Question 7: Does increased glucose monitoring in Type 2 patients improve clinical outcomes? More specifically, how confident are you that an increased frequency of out-patient glucose monitoring translates to decreases in chronic complications (specifically cardiovascular morbidity and mortality) in Medicare age patients (≥65 years) with type 2 and that the optimal frequency for glucose monitoring (number of strips per week, number of strips per day, or continuous) is known?

Very confident	Somewhat confident	Unsure	Somewhat unconfident	Very unconfident
5	4	3	2	1

Discussion Question:

- If changes in HbA1c do not predict changes in cardiovascular morbidity and mortality, what is the role for HbA1c in studies of glucose monitoring?