April 19, 2024

RE: Medicare & Medicaid Services' (CMS) Medicare Evidence Development & Coverage Advisory Committee (MEDCAC): Devices for Self-management of Type 1 and Insulin-Dependent Type 2 Diabetes

I appreciate the opportunity to comment on the Centers for Medicare & Medicaid Services' (CMS) Medicare Evidence Development & Coverage Advisory Committee (MEDCAC) meeting. By way of introduction, I am a senior clinician-investigator at the University of Washington School of Medicine in Seattle. I was an investigator in the first major CGM study in type 1 diabetes (the JDRF CGM study in 2008). I personally have type 1 diabetes (for 60 years), as do my brother and nephew. Like my patients, after this many decades of diabetes, hypoglycemia is asymptomatic, and without the CGM I am sure my brother nor I would not be alive right now. That is my medical opinion of myself, and more than 150 of my patients in the Medicare age group who have the same challenges as I do. In my brother's book "Cheating Destiny" he documented rolling his SUV over and into a ditch prior to the CGM era. One of the reasons we are seeing the explosion of childhood type 1 diabetes in the elderly is due to CGM and the avoidance of otherwise life-threatening hypoglycemia.

My comments, however, are not about the various surrogate endpoints or the reduction we have seen in severe hypoglycemia in the type 1 elderly. You will receive other documentation about those topics and how the CGM has revolutionized type 1 diabetes care. Rather, I would like to bring to your attention the topic of "high glycators" and "low glycators".

This topic has been mostly dormant for over 20 years. By way of background, there were several investigators comparing HbA1c with other metrics of diabetes. For example, investigators studied the "glycation gap", comparing fructosamine, another glycated product which is elevated in diabetes, to HbA1c. If there was a "gap", where the HbA1c was higher than expected than the fructosamine, more microvascular complications were observed. The theory is these "high glycators" were not only glycating hemoglobin, but also retina and glomerular proteins at a greater rate. The problem is like HbA1c, fructosamine also has many limitations. Other investigators studied discordance between home blood glucose levels and HbA1c. Again, when HbA1c was higher than expected with home blood glucose tests, more complications were seen.

UW Diabetes Institute

750 Republican Street
Building F, Floor 3
Seatt le, WA 98109

OFFICE 206.598.4882
FAX 206.598.8664
WEB uwmdi.org

This hypothesis was mostly forgotten as investigators from the DCCT/EDIC study showed that the "hemoglobin glycation index" (HGI) did not correlate with complications once adjusted to HbA1c. The HGI was calculated by the DCCT/EDIC group and other investigators by regression analysis by mean glucose levels measured by fingerstick 7-point glucose profiles. While other adjustments were made, the important point is these 7-point profiles over a 24-hour period do not provide nearly the amount of glycemic data as 14 or 28 days of CGM to calculate a glucose management indicator (GMI).

In 2022, a group from Italy showed more skin auto-florescence in "high glycators". This high-glycator group had more microvascular disease. We took this a step further and showed more retinopathy and renal disease in this high glycator group, which like the Italian group, we defined as a GMI/HbA1c < 0.9. We looked at a population of 640 subjects mostly with type 1 diabetes. The data have been presented but has not yet been peer-reviewed for publication (we plan to submit this shortly).

I decided to introduce this topic as part of "emerging evidence" of the potential use of CGM using the GMI. This metric measures thousands of glucose levels, not a 7-point glucose profile nor a glycated protein such as fructosamine which has many limitations. Continuous glucose monitoring (CGM) allows us to measure glucose, not a biomarker, and although our work is early, it points out to potential roles of CGM not yet appreciated by the scientific community.

We plan to continue our work with this "glycemic ratio" as we see no need for any complex statistical analysis (as needed to be done with infrequent glucose testing) to find high, or low glycators. While we appreciate all of the various surrogate endpoints your committee will be reviewing, I feel this endpoint needs to be considered as something we will have more definitive data in the next few years and will give clinicians (and patients) an even better understanding of their risk other than HbA1c or for that matter, perhaps time-in-range.

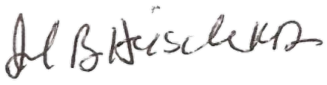
UW Diabetes Institute

750 Republican Street
Building F, Floor 3
Seatt le, WA 98109

OFFICE 206.598.4882
FAX 206.598.8664
WEB uwmdi.org

One final point. The DCCT would not have been possible without fingerstick glucose testing. Many people forget that before that, the patients with diabetes had no real way to check their blood sugars. While the DCCT (and later the UKPDS) are known as landmark studies showing how glucose control could impact microvascular complications, the cost was severe hypoglycemia. The DCCT showed rates of 62 events of severe hypoglycemia/100 patient-years. Today, those event rates (depending on the trial) are usually less than 10 events/100 patient years using CGM. While the glycation ratio is something I want the committee to understand, the hypoglycemia reduction we see today is an outcome that has changed insulin-using patients forever, and my only disappointment is that all patients who could benefit do not have access. Level 3 hypoglycemia to me is a most important endpoint, but difficult to quantify in a clinical trial. Using “big data” (payor or EMR databases such as Epic Cosmos) can certainly quantify this.
Thanks for allowing me to comment on this important matter.

Sincerely,



Irl B. Hirsch, MD
Professor of Medicine
University of Washington School of Medicine

UW Diabetes Institute

750 Republican Street
Building F, Floor 3
Seatt le, WA 98109

OFFICE 206.598.4882
FAX 206.598.8664
WEB uwmdi.org