$P = 0.05$) was observed when SDs of seven-point glycemic profiles were substituted for MAGE values.

Even though the MAGE determination requires continuous glucose monitoring, we believe that this parameter should be the "gold standard" for assessing glucose fluctuations in all prospective interventional studies designed to estimate glucose variability. We therefore believe that additional studies are required to definitively determine the role of glycemic variability in the pathogenesis of the micro- and macrovascular complications of diabetes. Even though the technology of continuous measurements of glucose in interstitial fluid remains a subject of debate, the use of continuous glucose sensors might be useful for conducting such trials.

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The Effect of Glucose Variability on the Risk of Microvascular Complications in Type 1 Diabetes

Response to Kilpatrick et al.

We have read with interest the article by Kilpatrick et al. (1), which reports the lack of effect of glucose variability on the risk for microvascular complications in type 1 diabetes using the Diabetes Control and Complications Trial database. We are pleased that the authors came to the same conclusions as we did in our examination (2) of this question using the same database. Since Diabetes Control and Complications Trial subjects were studied for differing durations and not all subjects provided complete seven-point glucose samples, how were these factors dealt with in the analysis? Furthermore, what were the reasons to limit the assessment of glucose variability to SD and omit measurements of M value and mean amplitude of glycemic excursion, two established indexes of glucose variability? The authors may wish to reexamine their literature research technique; it appears to be less than rigorous.

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The Effect of Glucose Variability on the Risk of Microvascular Complications in Type 1 Diabetes

Response to Kilpatrick et al. and Bolli

We read with interest the article by Kilpatrick et al. (1) and the accompanying editorial by Bolli (2). While the analysis of seven-point glucose profiles reported in this study (1) suggested that glucose variability is not an independent risk factor for microvascular complications, the seven-point profile may not be an accurate representation of true glycemic variability as measured by continuous blood glucose monitoring (3). Although there are not enough data at present to justify new treatment guidelines based on glycemic variability, there certainly are important published data (3) showing that glycemic variability leads to greater oxidative stress. Since increased intracellular superoxide production has been shown to initiate a large number of hyperglycemia-induced mechanisms related to the pathogenesis of diabetic complications (4), we believe that further investigation of the hypothesis that increased glycemic variability is a risk factor for diabetic complications is warranted.

Indeed, it was not that long ago that there was widespread doubt in the medical community that increased levels of hyperglycemia were a risk factor for diabetic complications (5). However, this doubt was addressed by further clinical research (6).

A little-noticed but very important observation published (6) by the Diabetes Control and Complications Trial Research Group >10 years ago was that sub-