Response to Cembrowski et al. regarding “Could Susceptibility to Low Hematocrit Interference Have Compromised the Results of the NICE-SUGAR Trial?”

To the Editor:

Cembrowski et al. (1) hypothesize that the hematocrit effect (i.e., the tendency of many blood glucose meter systems toward a positive bias at low hematocrits) in the SureStep®Flexx® device (LifeScan) may have caused false hyperglycemia, which, when treated with insulin, may have led to some of the hypoglycemic events observed in the NICE-SUGAR (Normoglycemia in Intensive Care Evaluation and Survival Using Glucose Algorithm Regulation) study.

We believe that the authors’ data do not support this assertion. First, the authors do not present any SureStep®Flexx® data related to hypoglycemic events, the hematocrit, or NICE-SUGAR. Therefore, there is no evidence that SureStep®Flexx® was associated with hypoglycemia during the NICE-SUGAR study.

Second, they show in their Fig. 1 that most of the data fell within the expected limits of ±20% accuracy. Indeed, the mean bias of the 3 test strip lots in question, compared with the Radiometer 800 blood gas analyzer, was 13.6%. The mean relative bias for these 3 test strip lots at lower glucose values was 0.83 mmol/L, vs the expected limits of ±1.0 mmol/L (±20 mg/dL). The authors do not state which, if any, of these data points were associated with the NICE-SUGAR study. Furthermore, the actual “trueness” of either glucose method is not known because laboratory glucose reference values are not provided.

Third, SureStep®Flexx® data points were included only when the sample was collected within 15 min of the blood gas analyzer sample. If the reason for this additional testing was a factor known to cause inaccuracies (e.g., operator error, hematocrit outside the labeled interval, shock, and so forth), then a difference between the 2 methods might be expected.

Finally, the authors concede that the NICE-SUGAR protocol contained many factors that might explain the increased prevalence of hypoglycemic events in the intensively treated group. The authors did not investigate these other factors, however, but instead chose to focus on the relative performance of 2 glucose methods.

In summary, the authors argue that a positive bias in SureStep®Flexx® measurement at low hematocrit values contributed to hypoglycemic episodes in the NICE-SUGAR study, but they do not present supportive evidence. A more cogent argument would have included details of hypoglycemic events along with the actual bias associated with the glucose-measuring device and the patient’s hematocrit. Because these data are not presented, the premise that a hematocrit effect, or device performance, caused hypoglycemic events in the NICE-SUGAR study is unfounded.

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