LETTER TO THE EDITOR

Response to Mitre et al.: “Analysis of Continuous Glucose Monitoring Data to Assess Outpatient Closed-Loop Studies: Considerations for Different Sensors”

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Dear Editor:

WE ARE THANKFUL TO Mitre et al.¹ for addressing the important issue of how to best measure outcomes during closed-loop studies. Mitre et al.¹ contrast four approaches: reference glucose, unmodified continuous glucose monitoring (CGM) data, stochastic transformation of CGM data, and their newly proposed CGM transformation to assess time in, time above, and time below target. We previously proposed the stochastic CGM transformation to correct for the bias introduced by the Navigator[®] CGM device (Abbott Diabetes Care, Alameda, CA) when using a single CGM device to direct closed-loop insulin delivery *and* simultaneously to assess outcomes.²

Like us, Mitre et al.¹ found that the use of unmodified CGM data, in their case obtained using the Sof-Sensor[®] probe (Medtronic Diabetes, Northridge, CA), leads to an overestimation of time in target during closed-loop but not during conventional pump therapy. Additionally, they document an underestimation of time above target during closed-loop. Thus Mitre et al.¹ concur with us in their generic findings but differ in the transformation needed to eliminate the bias. We are grateful to learn that the 15% measurement error we proposed for the Navigator is not applicable to the Sof-Sensor, which tends to underestimate glucose in hyperglycemia, and a simple mapping correction (4–8 mmol/L mapped to 4–7 mmol/L) is applicable.

The corrections proposed by Mitre et al.¹ and ourselves² are relatively simple to implement and are advisable for home or transitional studies of closed-loop systems when reference glucose measurements are not available. We are aware that these relatively simple transformations do not fully reflect the complex relationship between CGM and underlying plasma glucose across the physiological glucose range. Furthermore, it is possible that the CGM–plasma

glucose relationship (in mathematical terms the conditional probability of plasma glucose given CGM level) may be altered by closed-loop glucose control. Further research may be needed to clarify these issues and to increase confidence in outcomes derived from CGM levels. Finally, we acknowledge that according to Mitre et al.¹ the treatment effect defined as the difference between time in target during closed loop and conventional therapy is unbiased when using unmodified Sof-Sensor data. This is reassuring in case researchers decide to analyze outcomes using unmodified Sof-Sensor data but is not generalizable to other sensors and may prohibit comparison with studies using a different sensor.

Acknowledgments

This work was supported by the JDRF (grants 22-2006-1113, 22-2007-1801, 22-2009-801, 22-2009-802, and 22-2011-668), the National Institute of Diabetes and Digestive and Kidney Diseases (grant 1R01DK085621), Diabetes UK (grant BDA07/0003549), the European Commission Framework Program 7 (grant 247138), the NIHR Cambridge Biomedical Research Centre, and the Medical Research Council Centre for Obesity and Related Metabolic Diseases.

Author Disclosure Statement

R.H. reports having received speaker honoraria from Minimed Medtronic, Lifescan, Eli Lilly, and Novo Nordisk, serving on an advisory panel for Animas and Minimed Medtronic, receiving license fees from BBraun, and having served as a consultant to BBraun and Profil. R.H. also reports patent applications. M.N. declares no competing financial interests exist.

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