RESPONSE TO COMMENT ON PINSKER ET AL.

Randomized Crossover Comparison of Personalized MPC and PID Control Algorithms for the Artificial Pancreas. Diabetes Care 2016;39:1135–1142

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We thank Dr. Steil (1) for critically reviewing our study comparing model predictive control (MPC) and proportional integral derivative (PID) control for the artificial pancreas (2). We agree that MPC and PID both come in many variants and that there are many successful trials of PID control for automated insulin delivery. We acknowledged in our study that both controllers performed very well overall, even after the 65-g unannounced meal was accounted for, and did so with low rates of hypoglycemia.

We recognize the value in comparing results across different studies and want to emphasize that we did not intend to dismiss studies with different designs. However, it is not possible to have an equitable comparison of MPC versus PID controllers through such meta-analyses. Our study was specifically designed for as fair and balanced a comparison as possible between the controllers. As demonstrated by Lee and colleagues (3,4), we tuned the controllers for performance of glucose control, not insulin delivery. A benefit of predictive control is the ability to adjust the timing of insulin delivery based on a future predicted glucose level, as shown by MPC giving the same overall dose of insulin as PID but at different times (2).

With that in mind, the algorithms were designed using the same principles of model-based control development from an identical model (5). The controllers were designed to reflect the nominal form of PID and MPC. MPC, similar to PID, can come in different variations and with additional features, such as target zone, velocity weight, and asymmetric cost function, that can significantly improve performance over the controllers used in our study (2), where use of these features improved overall time in the target glucose range 70–180 mg/dL to 75% including exercise and 98.8% overnight (6). To enable an equitable comparison, we used a fairly generic version of each controller and only incorporated clinically validated features that compensate for insulin stacking (insulin feedback method for PID [7] and insulin on board for MPC [8]). The controllers were tuned using the Universities of Virginia and Padova simulator under identical conditions. The clinical protocol included challenges to the controller to evaluate both a typical day as well as the more challenging condition of an unannounced meal to better assess the readiness of these designs for extended use. The study design was randomized crossover to avoid bias and learning effects.

As noted in the detailed simulation study, the PID algorithm showed slightly better results in terms of the overall time in the safe glycemic range of 70–180 mg/dL, with lower peak glucose and mean glucose after both announced and unannounced meals, although this difference was not statistically significant (3,4). However, as was reported by Pinsker et al. (2), a study with 30 patients with type 1 diabetes, MPC showed an overall higher time in the target glucose range and ability to overcome an unannounced meal. Nevertheless, the overall performance of both algorithms was very good. It is likely for real-life use that variants of both algorithms will be used with success, as both perform better than the current open-loop care.

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Duality of Interest. J.B.L. is currently employed by the Insulet Corporation and completed the work for this clinical trial (2) during his Harvard/University of California, Santa Barbara, appointment. Insulet has licensed the MPC algorithm used in this study for future development. E.D. and F.J.D. have patents on the underlying MPC algorithms used in the study (2) and are currently receiving royalty payments on these patents. E.D. is a consultant to Insulet. H.C.Z. is currently employed by Verily Life Sciences and completed the work for this clinical trial (2) during his Sansum/University of California, Santa Barbara, appointment. No other potential conflicts of interest relevant to this article were reported.

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