



COMMENT ON PINSKER ET AL.

## Randomized Crossover Comparison of Personalized MPC and PID Control Algorithms for the Artificial Pancreas.

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Pinsker et al. (1) compare the performance of an artificial pancreas system using a model predictive control (MPC) algorithm of their own design to the performance of the same system using a proportional integral derivative (PID) algorithm, also of their own design. They conclude that MPC performs better. The authors emphasize that MPC “comes in many flavors” but do not acknowledge the same for PID (1). Using a PID controller of their own design rather than a version that has undergone numerous design iterations, such as the Medtronic algorithm (2,3) or an interacting PID algorithm developed at Boston Children’s Hospital (4,5), makes their study less than compelling.

The authors argue that they designed their MPC and PID algorithms to have “the same level of aggressiveness” but, by their own analysis, their PID algorithm required higher glucose values (mean 160 [SD 31.5] vs. 138 [20.4] mg/dL,  $P = 0.012$ ) to deliver the same total insulin (36.8 [9.29] vs. 38.9 [11.2] units PID vs. MPC, respectively,  $P = 0.535$ ) (1). Moreover, it is not only total insulin that counts but also when the insulin is delivered. Their PID algorithm suspended insulin delivery during meals before delivering sufficient insulin to cover the meal (see Fig. 2 in ref. 1, dinner), leading to more insulin being needed later in the meal when it is less effective. This can be corrected, without affecting total delivery, by shifting the insulin that is delivered during the meal to an earlier time point. Shifting to an earlier time can be achieved by increasing the

$\alpha$ -component of the PID response ( $\alpha$ -component adds insulin as glucose levels increase above target and subtracts same as the values return to target). Faster delivery can also be achieved by increasing insulin feedback (2). More evidence that the two controllers were not similarly aggressive can be seen during lunch, where their PID controller appears to deliver less insulin (see Fig. 2C) than their MPC controller despite higher glucose values (see Fig. 2B) (1). Here, delivery is reported as not different (MPC mean  $-3.71$  [SD 2.76] vs. PID  $-3.84$  [2.91],  $P = 0.92$ ) (see Supplementary Table 4), but it is unclear whether these values include delivery not shown in Fig. 2C (1). These observations suggest their PID controller was poorly configured, which similar to a poorly configured insulin pump, will result in poor control.

The authors correctly assert that results from different studies cannot be directly compared; however, they cannot completely dismiss artificial pancreas studies conducted with different PID designs that show better performance at multiple sites and patient populations. Particularly studies that use larger meals (e.g., 96 g carbohydrate, 60 fat, 39 protein dinner [4] vs. 65 g carbohydrate dinner [1]), rely less on meal announcement to deliver insulin (e.g., no meal announcement [5], 2 units unrelated to carbohydrate count [2] vs. bolus calculated from insulin-to-carbohydrate ratio [1]), and have not reported any instances where control needed to be suspended (compare with one anecdotal report [1]). Thus, while the authors can

justifiably conclude their MPC algorithm performs better than their PID algorithm, they cannot extend this conclusion to include all PID algorithms. Equipose is advised.

**Duality of Interest.** G.M.S. is a former employee of Medtronic and listed as inventor on several Medtronic patents related to the artificial pancreas; however, he has no financial interest in these patents (rights assigned to Medtronic) and has no financial relationship with the company. G.M.S. has performed consulting for Roche Diagnostics and BD medical devices and receives device support from Dexcom for a study assessing the effect of daytime activity on nighttime insulin requirement. No other potential conflicts of interest relevant to this article were reported.

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