LETTER

Cost-Effectiveness of Intermittently Scanned Continuous Glucose Monitoring Versus Advanced Hybrid Closed-Loop Systems in Type 1 Diabetes: Comment on Jendle et al.

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A recent publication in *Diabetes Therapy* from Jendle and colleagues [1] reports on the cost-effectiveness of the MiniMed 780G advanced hybrid closed-loop (AHCL) system (Medtronic, Northridge, CA) in people with type 1 diabetes (T1DM) in Sweden, by comparison with the intermittently scanned FreeStyle Libre® flash glucose monitoring system (Abbott, Witney, UK) when used in conjunction with multiple daily insulin injections (MDI) or with continuous subcutaneous insulin infusion (CSII). The authors conclude that the MiniMed 780G AHCL is cost-effective compared to the FreeStyle Libre system plus MDI or CSII for treating people with T1DM. We must argue that this conclusion depends on modelling assumptions that have the potential to introduce bias into the

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assignment of value to health-state utilities as part of cost-effectiveness models [2].

Firstly, the authors claim reduced incidence and delayed time to onset of diabetes-related complications for the AHCL system versus the FreeStyle Libre system plus MDI or CSII, based on the treatment effects of each system, documented in only two selected studies [3, 4]. In the first, a randomized clinical trial (RCT) [3], the authors assert a reduction in HbA1c of − 0.5% (− 5.5 mmol/mol) for the MiniMed 780G system, when used in the 4-week intervention phase. However, this is not reported in the outcomes data or supplementary materials, which focus on increased time in range (TIR) 3.9–10 mmol/L and reduced average glucose. Although these are reported to correlate to a glucose management indicator (GMI) of 6.8% in the intervention arm, this should not necessarily be assumed to be equivalent to change in long-term laboratory HbA1c, which can differ significantly [5]. They then cite the 6–12-month outcomes from the FUTURE study [4] as evidence of no change in HbA1c from baseline using the FreeStyle Libre system in T1DM. By making the extrapolation from improved sensor-glucose metrics to a change in HbA1c from a 4-week RCT intervention [3] and comparing it with observed HbA1c outcomes from a single 12-month real-world study [4] is unrealistic in a cost-effectiveness calculation. There are no head-to-head studies that assess the two

interventions on comparable populations over comparable timeframes, which means the analysis presented is highly subjective, rather than objective. The RCT cohort ($n = 60$) is 58% female, has defined inclusion criteria and has a mean age of 23.5 years, with a mean 13.2 years duration of diabetes, which reflects the inclusion of 33 children and adolescents aged 7–21 years [3]. The FUTURE study includes 1913 consecutive adults [4], with 46% female, a mean age of 45.8 years and 22.8 years duration of diabetes. Independent from these discrepancies, the 4-week data from the RCT on its own cannot be reliably extrapolated to 12 months, thus depriving the analysis of generalizability. It is worth pointing out that a wide range of real-world studies have consistently reported reductions in HbA1c in T1DM with continuous glucose monitoring (CGM), including the Free-Style Libre system, which is correlated with baseline HbA1c [6, 7]. For example, use of the FreeStyle Libre system in T1DM is associated with reductions of -0.75% (8.2 mmol/mol; $p < 0.001$) at 3 months [8] compared to blood-glucose monitoring, which is sustained at 12 months. The authors could use the available meta-analysis of real-world HbA1c reductions using the FreeStyle Libre system [7] to model the comparative value in this context.

These concerns also introduce bias into the claims regarding severe hypoglycemic events (SHE) which use a zero rate for the AHCL system and 63.9 events/100 patient years for the Free-Style Libre system, based on comparison of the same non-comparable studies [3, 4]. No objective relationship can exist between lack of SHEs in a small-scale RCT with a 4-week intervention phase and the rate of SHEs in a much larger 12-month real-world study, given the lack of comparable study parameters and differences in patient populations.

The issues outlined above are accompanied by a lack of sensitivity analysis, which is performed only for HbA1c against changes in the base case for the AHCL system and mainly predicated on further reductions in HbA1c. The incidence and cost of SHEs were not subject to sensitivity analysis, yet the health-related utility of reduced SHEs in the base case is weighted in favour of the AHCL system in calculating quality-of-life (QOL) benefits arising from reduced fear of hypoglycemia (FOH). Notably, the value of this utility is founded in outcomes from the INTERPRET study, itself using CGM in sensor-augmented pump therapy [9], and the algorithm used to calculate the utility of reduced FOH was developed using data available only up to 2006 [10]. Since this utility is a key driver of the IQVIA Core Diabetes Model, this is a significant oversight given the available evidence for improved QOL and reduced FOH for people with T1DM using the FreeStyle Libre system [11].

Within the limitations identified, we do acknowledge the need for objective cost–benefit assessments for diabetes management technologies within healthcare economies. The authors of this paper have identified both the opportunity to further these aims and also the need for the application of consistent datasets, where available. However, the biases and assumptions within their analysis need to be considered in this wider context.

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REFERENCES

1. Jendle J, Buompensiere MI, Holm AL, de Portu S, Malkin SJP, Cohen O. The cost-effectiveness of an advanced hybrid closed-loop system in people with type 1 diabetes: a health economic analysis in Sweden. Diabetes Ther. 2021. https://doi.org/10.1007/s13300-021-01157-0.

2. Brazier J, Ara R, Azzabi I, et al. Identification, review, and use of health state utilities in cost-effectiveness models: an ISPOR good practices for outcomes research task force report. Value Health. 2019;22:267–75. https://doi.org/10.1016/j.jval.2019.01.004.

3. Collyns OJ, Meier RA, Betts ZL, et al. Improved glycemic outcomes with Medtronic MiniMed advanced hybrid closed-loop delivery: results from a randomized crossover trial comparing automated insulin delivery with predictive low glucose suspend in people with type 1 diabetes. Diabetes Care. 2021;44:969–75.

4. Charleer S, Block CD, Huffel LV, et al. Quality of life and glucose control after 1 year of nationwide reimbursement of intermittently scanned continuous glucose monitoring in adults living with type 1 diabetes (FUTURE): a prospective observational real-world cohort study. Diabetes Care. 2020;43:389–97.

5. Bergenstal RM, Beck RW, Close KL, et al. Glucose management indicator (GMI): a new term for estimating A1C from continuous glucose monitoring. Diabetes Care. 2018;41:2275–80.

6. Gilbert TR, Noar A, Blalock O, Polonsky WH. Change in hemoglobin A1c and quality of life with real-time continuous glucose monitoring use by people with insulin-treated diabetes in the landmark study. Diabetes Technol Ther. 2021;23:S-35-S-39.

7. Evans M, Welsh Z, Ells S, Seibold A. The impact of flash glucose monitoring on glycaemic control as measured by HbA1c: a meta-analysis of clinical trials and real-world observational studies. Diabetes Ther. 2019;11:83–95.

8. Rose L, Klausmann G, Seibold A. Improving HbA1c control in type 1 or type 2 diabetes using flash glucose monitoring: a retrospective observational analysis in two German centres. Diabetes Ther. 2021;12:363–72.

9. Nørgaard K, Scaramuzza A, Bratina N, et al. Routine sensor-augmented pump therapy in type 1 diabetes: the INTERPRET study. Diabetes Technol Ther. 2013;15:273–80.

10. Currie CJ, Morgan CL, Poole CD, Sharplin P, Lammert M, McEwan P. Multivariate models of health related utility and the fear of hypoglycaemia in people with diabetes. Curr Med Res Opin. 2006;22:1523–34.

11. Hayek AAA, Robert AA, Dawish MAA. Evaluation of FreeStyle Libre flash glucose monitoring system on glycemic control, health-related quality of life, and fear of hypoglycemia in patients with type 1 diabetes. Clin Med Insights Endocrinol Diabetes. 2017. https://doi.org/10.1177/1179551417746957.