Can continuous glucose monitoring technology reduce fear of hypoglycemia in people with type 1 diabetes?

To the editor We read with interest the recent paper by Kłak et al[1] published in *Polish Archives of Internal Medicine* (*Pol Arch Intern Med*). We would like to thank the authors for their timely contribution to the literature via a review of the current evidence for the impact of continuous glucose monitoring (CGM) on patient-reported outcomes, including fear of hypoglycemia. Overall, while the authors presented interesting results suggesting that CGM reduces fear of hypoglycemia and improves the quality of life, we have some concerns, as outlined below.

First, while the authors declared their population of interest to be individuals with type 1 diabetes, they included a study[2] with a mixed sample of patients both with type 1 and type 2 diabetes, without discussing the trade-off between including studies with participants not exactly meeting the eligibility criteria and the loss of data when excluding them.[3]

Additionally, 3 of the 6 studies included in the analysis of the Hypoglycemia Fear Survey--Worry subscale scores do not seem to satisfy the intervention criteria presented in the *Methods* section. The authors defined the intervention as any type of CGM system, and conventional self-measurement of blood glucose using glucometers as the control. Kropf et al (*Diabet Med*, 2017) compared sensor-augmented pump with an artificial pancreas system (2 advanced diabetes technologies enabling a connection between a CGM system and an insulin pump),[4] Reddy et al (*Diabetes Technol Ther*, 2018) considered an intermittently scanned CGM (flash glucose monitor) as a control compared with real-time CGM (rtCGM) as the intervention, and Walker et al (*J Diabetes Sci Technol*, 2014) compared a fully functional rtCGM as a control to a blinded rtCGM (intervention).

Other concerns pertaining to this manuscript include not accounting for baseline levels of fear of hypoglycemia in the meta-analysis, which could be misleading. For example, when considering the study by Reddy et al, the authors of the review reported higher fear in the intervention group compared with controls, without acknowledging that baseline fear of hypoglycemia was higher in the intervention group.

Furthermore, 3 studies were excluded from the review due to the lack of a control group, yet one of these was a randomized, controlled, crossover study (Hommel et al; *Acta Diabetol*, 2014), which indicates the presence of a control group. The other 2 studies were prospective, observational studies with a total of 694 adult participants (Charleer et al; *J Clin Endocrinol Metab*, 2018 and Nørgaard et al; *Diabetes Technol Ther*, 2013). The authors included a cross-sectional study,[2] yet decided to exclude these 2 prospective studies that could add real-life insights on the temporality of the association observed between technology use and the outcomes.

In conclusion, while Kłak et al[1] presented interesting results summarizing some of the literature data on the important topic of diabetes technologies and fear of hypoglycemia, certain methodological aspects might need further consideration.

ARTICLE INFORMATION

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CONFLICT OF INTEREST The authors of this letter are currently working on a review on the topic of diabetes technologies use and impact on fear of hypoglycemia in type 1 diabetes, registered as PROSPERO 2021 CRD42021253618.

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1 Kłak A, Mańczak M, Owoc J, Olszewski R. Impact of continuous glucose monitoring on improving emotional well-being among adults with type 1 diabetes mellitus: a systematic review and meta-analysis. Pol Arch Intern Med. 2021; 131: 808-818.

2 Polonsky WH, Peters AL, Hessler D. The impact of real-time continuous glucose monitoring in patients 65 years and older. J Diabetes Sci Technol. 2016; 10: 892-897.

3 McKenzie JE, Brennan SE, Ryan RE, et al. Defining the criteria for including studies and how they will be grouped for the synthesis. In: Higgins JPT, Thomas J, Chandler J, et al, eds. Cochrane Handbook for Systematic Reviews of Interventions. 2nd Edition. Chichester (UK): John Wiley & Sons; 2019: 33-65.

4 American Diabetes Association. 7. Diabetes technology: standards of medical care in diabetes – 2021. Diabetes Care. 2021; 44 (Suppl 1): S85-S99.

Authors' reply We appreciate the letter by Talbo et al[1] regarding our article.[2] We would like to thank the authors for their careful and detailed analysis and kindly reply to their concerns.

Polonsky et al[3] indeed studied both patients with type 1 and type 2 diabetes. However, the latter group of participants accounted for only 8.8% of the entire sample, which, in our opinion, made this study suitable for analysis. Also, the small number of studies eligible for quantitative analysis encouraged us to include this particular study. Likewise, its exclusion would adversely affect the comprehensiveness of our review. Nevertheless, we undoubtedly should have referred to the issue of a mixed study sample in the manuscript and regret overlooking this. Still, we believe it did not have any impact on the conclusions or overall results of the study.

The original version of the manuscript included the following statement: *Conventional self-monitoring of blood glucose (SMBG) was defined as measuring blood glucose by finger-capillary blood sample at least once a day. The glucose level was measured using a blood glucose meter* and *other types of continuous glucose monitoring system*. As the final version was the result of many comments, suggestions, and discussions with reviewers, it is most likely that last part of the second sentence was somehow overlooked at some stage. Yet, this information was still included in Table 1 in the column referring to the control group (*Control group [eg. SMBG or blinded CGM]*).

The manuscript contains the following sentence: *The only exception was the study by Reddy et al* (Diabetes Technol Ther, *2018), in which higher scores on the total HFS-II scale, HFS-W and HFS-B subscales, and the Problem Areas in Diabetes Scale (PAIDS) were found in the CGM group*. Although we did not say in the main part of the manuscript that the initial level of fear of hypoglycemia was higher in the intervention group, you may still find this information in Supplementary material, *Table S5*.

Results regarding the quality of life in the study by Hommel et al (*Acta Diabetol*, 2014) were not presented very clearly and transparently. They are included in Table 2, which is not transparent and fairly difficult to comprehend because it shows change versus baseline for both groups simultaneously: in the sensor-on arm compared with the sensor-off arm. However, in Table 1 you can find results on the self-reported health-related quality of life in children compared with their parents' proxy ratings. In the study by Charleer et al (*J Clin Endocrinol Metab*, 2018), the intervention group comprised adults with type 1 diabetes from the Belgian RT-CGM reimbursement program who were on continuous subcutaneous insulin infusion therapy. The control group consisted of patients who had started the treatment before the program was introduced. It is not clearly stated in the study whether these participants ever used a commercial RT-CGM or not before the program started.

The study by Nørgaard et al (*Diabetes Technol Ther*, 2013) was a 12-month observational study in patients with type 1 diabetes treated with continuous subcutaneous insulin infusion therapy upon the introduction of continuous glucose monitoring systems. It had no control group. The cross-sectional study[3] was a questionnaire survey research which met our inclusion criteria.

We would like to thank Talbo et al[1] for their valuable insight. Indeed, some aspects presented in the *Discussion* section and other elements should have been elaborated on more precisely. However, we remain convinced that it did not affect the results and conclusions of our study. We also would like to emphasize that until the moment of publication, there was no meta-analysis that would comprehensively focus on the quality of life and fear of hypoglycemia in adults with type 1 diabetes. The methodology proved to be challenging, and this is probably one of the reasons why no such work was done earlier. We used our best efforts to make our review reliable and appropriate in academic terms. It must be kept in mind, though, that every study carries a risk of bias and methodological inaccuracies.[4]

ARTICLE INFORMATION

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