



RESPONSE TO COMMENT ON ZU ET AL.

## Association of Body Weight Time in Target Range With the Risk of Kidney Outcomes in Patients With Overweight/Obesity and Type 2 Diabetes Mellitus.

Diabetes Care 2024;47:371–378

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Diabetes Care 2024;47:e85–e86 | <https://doi.org/10.2337/dci24-0065>

We thank Groothof et al. (1) for their insightful comments on our recent article published in *Diabetes Care* (2). We fully agree with Groothof et al. that more evidence is needed to evaluate the relationship between body weight time in target range (TTR) and estimated glomerular filtration rate (eGFR). Our response to these comments is as follows.

First, as Groothof et al. (1) mentioned, a common limitation of using creatinine-based eGFR in weight loss studies is that it may be overestimated due to reduced serum creatinine levels during muscle weight loss (3). However, we have also evaluated the association of body weight TTR with the risk of very-high-risk chronic kidney disease (4), a doubling of urine albumin-to-creatinine ratio from  $<10$  mg/g to  $\geq 10$  mg/g (5), and a doubling of urine albumin-to-creatinine ratio from  $<30$  mg/g to  $\geq 30$  mg/g (5), and we found similar results, suggesting a definite association between body weight TTR and kidney prognosis in patients with overweight/obesity and type 2 diabetes.

Second, the suggestion of Groothof et al. (1) to use serum cystatin C as a proxy to calculate GFR is reasonable. Cystatin C is less affected by muscle mass and could provide a more stable

estimation of kidney function, especially in people undergoing weight loss. We agree that reassessing the relationship between weight TTR and composite kidney outcome based on cystatin C–based eGFR might yield more accurate results (6). Unfortunately, in the Look AHEAD study, data on cystatin C were unavailable, and only a small subset of participants had C-reactive protein measurements at baseline and in the first year of the study. The lack of these data limited our further exploration of the relationship between body weight TTR and kidney function estimated using serum cystatin C. Therefore, future studies are needed to examine the relationship between weight TTR and kidney outcomes, in particular calculating eGFR based on both cystatin C and serum creatinine to address the issue of eGFR overestimation due to muscle mass loss. Additionally, the relationship between body weight TTR and inflammatory markers, including C-reactive protein, needs to be further explored to more fully understand the impact of weight management on kidney function.

Overall, as we mentioned in our article (2), the relationship between body weight TTR and kidney outcomes is hypothesis generating and should be interpreted

with caution. We appreciate the constructive feedback from Groothof et al. and will consider these suggestions in future studies. Their recommendations will help enhance the rigor of our research findings and contribute to a more detailed understanding of the relationship between body weight TTR and kidney health.

**Duality of Interest.** No potential conflicts of interest relevant to this article were reported.

**Handling Editors.** The journal editor responsible for overseeing the review of the manuscript was Steven E. Kahn.

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