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Diabetic kidneys do deserve a lifestyle change

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De Zeeuw and Lambers Heerspink comment on our report of lower nephropathy incidence with intensive lifestyle intervention in the Look AHEAD clinical trial in type 2 diabetes.¹ They write that we reported a secondary analysis of an outcome not specifically defined in the protocol, as clearly acknowledged in the paper. Although there were no differences in the primary outcome—cardiovascular events², our secondary analysis is also informative because a broad range of health effects should be considered in evaluating an intervention, with nephropathy unquestionably important in diabetes. Treatment decisions are based on many factors beyond a “primary outcome”.

These writers suggest that we should have reported end-stage renal disease (ESRD) or doubling of serum creatinine, because they are conventional primary outcomes in clinical trials of late renal disease. Further, they ask why lifestyle intervention should not require the same level of evidence for ESRD as for drug approval. We believe recommending lifestyle change, which is generally safe and has many known benefits, need not wait for conclusive evidence of prevention of ESRD. These authors recently suggested using microalbuminuria as an endpoint, because late outcomes including ESRD are of limited value in trials in early disease.³ Consistent with their suggestion, we evaluated albuminuria, which was significantly lower with lifestyle intervention. As Look AHEAD participants had a median duration of known diabetes of only five years and no overt renal disease at entry, few developed ESRD, which typically occurs after decades of diabetes. Our reported effects on ESRD and doubling of serum creatinine are consistent with those on earlier renal outcomes, but with wide confidence intervals due to the small number of events. The consistency among these outcomes strengthens our conclusion that lifestyle change benefits the kidneys in type 2 diabetes, although as noted by de Zeeuw and Lambers Heerspink, the mechanism of the renal protective mechanism of weight loss remains to be determined.

References

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