

Evaluating a Type 2 Diabetes Prevention Program

NCT: 5822648

04/16/2023

Analyses. For the continuous response variables in Aims 1 and 2 we will fit linear mixed effects models (LME) or generalized additive models (GAM) if change across the study is nonlinear. All models will include an interaction of time since the start of the study (in months) and condition (as well as all lower-order main effects). For both LMEs and GAMs, we will control for the lack of independence between the observations within a participant by including random intercepts and random slopes (if necessary) for the participants in our models and for participants nested within groups.

To detect for differences in the onset of T2D (Aim 1) between the intervention and control condition, we will fit a Cox proportional hazard model using the survival package (Therneau, 2022) in R. The proportional hazard assumption will be assessed and in the event of violations of this assumption, stratified proportional hazard models will be fit.

For the mediation analysis for Aim 2, the mediation package (Tingley et al., 2014) in R will be used to employ the causal mediation approach described in Imai et al. (2010). This is a more general and flexible causal mediation framework than the traditional structural equation modeling approach to mediation. Specifically, this approach enables (1) definitions of causal mediation effects that are independent of a particular statistical model, (2) specification of the identifiability assumption, and (3) a framework that can be applied to a myriad of models (most importantly for this study, LMEs, GAMs, and survival models). In addition, sensitivity analyses can be conducted to explore the sequential ignorability assumption. Using this framework involves modeling the onset of T2D via a parametric survival regression model that includes condition and the proposed mediator (percent body fat). This model's output is then combined with the mediator model's output, the percent body fat model from Aim 1, and used to calculate the average causal mediation effect (ACME), the proportion of the total effect that is mediated as well as other mediation statistics, which can then be tested using either quasi-Bayesian Monte Carlo or the non-parametric bootstrap.

## References

Tingley, D., Yamamoto, T., Hirose, K., Keele, L., & Imai, K. (2014). mediation: R Package for Causal Mediation Analysis. *Journal of Statistical Software*, 59(5), 1–38.  
<https://doi.org/10.18637/jss.v059.i05>