Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

HHS Public Access

Author manuscript

J Epidemiol Community Health. Author manuscript; available in PMC 2025 August 19.

Published in final edited form as:

J Epidemiol Community Health. ; 79(12): 900–906. doi:10.1136/jech-2025-224037.

Heterogeneity in Associations between Food Insecurity and Diabetes Outcomes

Seth A. Berkowitz, MD MPH[1,2,3], **Mufeng Gao, MSc**[4], **Aileen Ochoa, MPH**[5], **Marlena L. Kuhn, MPH**[6], **Jenine Dankovchik, BSc**[5], **Jenna M. Donovan, MPH**[5], **Myklynn LaPoint, BA**[2,3], **Sanjay Basu, MD PhD**[7], **Michael G. Hudgens, PhD**[4], **Rachel Gold, PhD MPH**[5,8]

[1]Division of General Medicine and Clinical Epidemiology, Department of Medicine, University of North Carolina at Chapel Hill School of Medicine, Chapel Hill, NC

[2]Center for Health Promotion and Disease Prevention, University of North Carolina at Chapel Hill School of Medicine, Chapel Hill, NC

[3]Cecil G. Sheps Center for Health Services Research, University of North Carolina at Chapel Hill, Chapel Hill, NC

[4]Department of Biostatistics, University of North Carolina at Chapel Hill, Chapel Hill, NC.

[5]Department of Research, OCHIN, Portland, OR

[6]Department of Social Medicine, Center for Health Equity Research, University of North Carolina at Chapel Hill, Chapel Hill, NC

[7]Clinical Product Development, Waymark Care, San Francisco, California

[8]Kaiser Permanente Northwest Center for Health Research, Portland, OR, USA

Abstract

Background: Food insecurity is associated with worse diabetes outcomes, but how that association may vary across individuals is unclear. We sought to better understand possible heterogeneity in the association between food insecurity and diabetes outcomes.

Methods: Longitudinal cohort study of adults with type 2 diabetes assessed for food insecurity in community-based health centers. Diabetes outcomes were hemoglobin A1c (HbA1c), systolic and diastolic blood pressure, and low-density lipoprotein cholesterol (LDL), 12 months after food insecurity assessment. We used three machine learning methods (generalized random

Address for correspondence: Seth A. Berkowitz, MD MPH, 5034 Old Clinic Bldg, CB 7110, Chapel Hill, NC 27599, seth_berkowitz@med.unc.edu.

Contributorship Statement:SAB made substantial contributions to the conception and design of the study and the acquisition, analysis, and interpretation of data for the study, and drafted the manuscript. RG and SB made substantial contributions to the conception and design of the study and the acquisition, analysis, and interpretation of data for the study, and revised the manuscript. MAL made substantial contributions to the interpretation of data for the manuscript and reviewing the manuscript critically for important intellectual content. MGH, MLK, and MG contributed to the analysis and interpretation of the data and reviewed the manuscript. AO, JMD, and JDD designed and built the datasets, contributed to the conceptual understanding of the underlying EHR data, and reviewed the manuscript.

Guarantor:SAB is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Ethics Statement

This study was approved by the institutional review board at the University of North Carolina at Chapel Hill (IRB# 21-2373).

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

forest [GRF], X-Learner, and DR-Learner) to assess outcome heterogeneity across the following variables: age, sex, race and ethnicity, health insurance, income, comorbidity, baseline outcome, and social vulnerability index.

Results: Among 41,581 individuals (mean age 56.2 [SD: 12.8] years, 56.9% female), mean baseline HbA1c was 7.8% (SD: 1.9%) and 10,399 (25.0%) reported food insecurity. Food insecurity was associated with 0.1% greater HbA1c at 12 months, with little heterogeneity. For example, using GRF, the mean difference in HbA1c in the quartile with the lowest estimated HbA1c difference associated with experiencing, versus not experiencing, food insecurity was 0.0%, while the mean difference in the quartile with the greatest estimated difference was 0.2%. Results were similar for other outcomes, except there was no association between food insecurity and LDL.

Conclusions: In this study, we did not observe meaningful heterogeneity in the associations between food insecurity and diabetes outcomes.

Food insecurity, lack of consistent access or uncertainty in access to the food needed for an active, healthy life, is associated with numerous poor health outcomes.[1-4] Food insecurity affected 14.1% of Americans in 2023, or over 47 million individuals.[1] Among individuals with type 2 diabetes mellitus (T2DM), food insecurity is associated with higher hemoglobin A1c, blood pressure, and low-density lipoprotein cholesterol (LDL) levels, on average.[2-6] Possible pathways for this connection include: incentivizing consumption of less expensive but less healthful foods; tradeoffs between affording medications and affording healthful foods; and the stress of experiencing food insecurity.[4,7,8] It is therefore plausible that interventions to address food insecurity may improve T2DM outcomes. However, some food insecurity interventions tested in randomized clinical trials have not shown clear benefit, as the trials found modest differences between study arms that were not statistically significant.[9,10] Moreover, a recent observational study had similar findings, in line with estimates from randomized trials.[11]

There are several possible explanations for modest average differences between arms in studies of food insecurity interventions in T2DM. One is that addressing food insecurity on its own only has a small impact on T2DM outcomes for all people. Another is that two equally sized subgroups have offsetting associations (e.g., strongly positive for one, and strongly negative for another). A third possibility is that a small subgroup has a strong association that, because of its size, has only a modest impact on the overall association (e.g., a strong positive association for a small subgroup, and a weak association for the majority of individuals). Distinguishing between these possibilities is important, as it can inform the design of future interventions, particularly the utility of targeting the intervention to specific individuals.

One common way to investigate heterogeneity of associations is to analyze results by subgroups, such as racial and ethnic identity or sex. This approach has drawbacks, including typically exploring only a single variable at a time rather than combinations of characteristics, and ignoring potential non-linearities in the relationship between relevant variables and the outcomes.[12-15] Recent advances in statistical methods for such ‘heterogeneous treatment effect’ (HTE) estimation use machine learning approaches

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

to overcome these limitations.[16-18] In this study, we applied recently developed HTE methods to understand heterogeneity in the relationship between food insecurity and T2DM outcomes. Though such methods would ideally be applied to randomized clinical trial data, to date no randomized clinical trials have had sufficient sample sizes to comprehensively investigate heterogeneity. Therefore, we used a large observational dataset in exploratory analyses to help guide the design of future interventions.

This study sought to identify situations in which food insecurity represents a more or less important barrier to better T2DM outcomes. Such variation may occur when people face barriers to T2DM management in addition to food insecurity, so that addressing food insecurity alone may have less impact. To that end, this study: 1) examined variation in the associations between food insecurity and T2DM outcomes, and 2) explored characteristics associated with greater and lesser estimated difference in T2DM outcomes associated with food insecurity.

Methods

Data Source and Study Setting

Data came from electronic health record hosted by OCHIN, Inc. (not an acronym), a provider of a centralized electronic health record system for community-based health centers across the U.S. The population for this study was adults with T2DM seen in community-based health centers. We included all adults (age ≥ 18 years) in the OCHIN dataset with T2DM (determined by previously validated algorithm—Technical Appendix) who had at least one food insecurity assessment[11,19-21] in the period of study (June 24th, 2016 to April 30th, 2023).

Exposure

The exposure of interest was reporting food insecurity, or reporting food security, at initial food insecurity assessment. In the OCHIN clinics' shared electronic health record, several food insecurity assessment tools are used.[11] The most common include items from the PRAPARE (Protocol for Responding to & Assessing Patients' Assets, Risks & Experiences) and Accountable Health Communities Health-Related Social Needs screening tools.[22,23] Both have been validated as performing well in comparison with the 18-item USDA household food security survey module.[24] The USDA module is considered the gold standard of food security assessment, but is rarely used in routine care given its length and respondent burden. Thus, the brief food insecurity assessments used in this study are those that are commonly used in routine clinical care to determine the need for food insecurity interventions.

Outcomes

The primary outcome for this study was hemoglobin A1c (HbA1c). Secondary outcomes were systolic blood pressure (SBP), diastolic blood pressure (DBP), and LDL. The timepoint of interest was 12 months after the initial food insecurity assessment during the study period. To operationalize this within electronic health record data, outcomes were computed as the mean of all assessments for that outcome made in the 6-12 months after the 'index date'

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

(date of initial food insecurity assessment). Individuals with no outcome recorded within this time window were not included in analyses of that outcome, but could be included in analyses of another outcome recorded in that period (e.g., if an individual had a blood pressure but not an LDL cholesterol recorded in the time window, they would be included in the blood pressure analyses but not in the LDL analyses).

Covariates

We considered several covariates that could affect the relationship between food insecurity and study outcomes. We used electronic health record data for following variables as of the date of initial food insecurity assessment: age, sex (recognizing that electronic health record assessment often imperfectly distinguishes between sex and gender), race and ethnicity, health insurance, income, an ICD-10 based comorbidity index,[25] and the mean value of the outcome in the year prior to food insecurity assessment. Using address data, we created a variable for the social vulnerability index (SVI) score of the census tract of residence, which reflects area-based socioeconomic exposures.[26] In sensitivity analyses, we also included body mass index (BMI) as a covariate.

Statistical Analysis

For statistical analysis, our goal was to estimate, using observational data, the difference in study outcomes at 12 months that may have occurred if individuals in the study had versus had not experienced food insecurity at their initial assessment. Moreover, we sought to explore whether and how those estimates varied across different combinations of covariates that could affect the relationship between food insecurity and the study outcomes. To do this, we used three different approaches that estimate ‘potential outcomes’ (outcomes that may have occurred under different counterfactual exposure scenarios) and ‘conditional average treatment effects’ (CATEs—the estimated difference in outcomes under different exposure scenarios conditional on the specific combination of individual covariates). Under the assumptions of conditional exchangeability, positivity, and consistency, these estimates can have a causal interpretation, and when discussing the *methods* used here we use terms like ‘HTE’ and ‘CATE’ to retain consistency with the broader literature on this topic. However, because we do not know that causal inference assumptions were met in this observational study, in interpretation of this study’s *results* we consider findings to be associations. We view these as exploratory, hypothesisgenerating findings to be studied further.

To aid in exploring potential heterogeneity in the association between food insecurity and the study outcomes, we used three different analytic approaches. We reasoned that if different methods found similar results, it would be a stronger signal of true heterogeneity, while if different methods had different results, it may be more suggestive of chance differences without clear heterogeneity. The three methods used were generalized random forests[27], X-learner[17], and DR-Learner.[28] We describe each of these methods briefly below, and provided references include more technical details.

Generalized random forest (GRF) is a non-parametric, tree-based approach to HTE estimation.[27] In brief, the approach randomly samples observations and variables within a data set to grow a ‘tree’ based on splitting the sample at a value of a variable that

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

minimizes a loss function (e.g., mean squared error), in order to model the relationship between exposure, covariates, and the outcome. This process is then repeated many times to grow a 'forest' of such trees. This 'forest' can then be used to estimate what an individual's outcome would have been under the scenario in which they experienced food insecurity, and the scenario in which they did not, which can then be contrasted. We fit forests of 2,000 trees.

The X-learner approach starts by fitting two separate models predicting the outcome—one using data from the exposure group (i.e., those who experienced food insecurity) and one using data from the comparison group (i.e., those who did not experience food insecurity).[17] It then uses those models to impute the unobserved potential outcome (i.e., for those who experienced food insecurity, an estimate of what their outcome would have been if they had not experienced food insecurity, and vice versa). Next, an estimate of the treatment effect is created by taking the difference of two outcomes—the observed outcome under the exposure the individual experienced (food insecure or secure), and the estimated outcome had they experienced the other exposure. Then another two models are created, one using treatment group data and one using comparison group data, but this time the treatment effect estimated in the prior step is modeled. From these models, two new estimates of the treatment effect for each individual are produced, one using the treatment group model and one using the comparison group model. Next, a propensity model is created to estimate the probability of the exposure (i.e., experiencing food insecurity). Finally, the two treatment effects from the second step are combined as a weighted average to create a single estimate per individual, with the weights being a function of the propensity score.

DR-learner is an estimator of HTE that, like X-learner, relies on estimating two quantities of interest—the outcome under different scenarios, and the propensity score.[28] DR-learner allows for an approach to estimating the outcome and propensity score called 'SuperLearning' which creates a weighted average of estimates produced using multiple machine learning methods.[29] With DR-learner, estimates of the outcome and propensity score can be made using several machine learning methods; then cross-validation is used to find a weighted average of estimates, each made using a different approach, that minimizes a loss function (such as mean squared error). This study implemented a SuperLearner approach that combined estimates from generalized linear models, generalized additive models, ridge regression, random forest implemented by R package *ranger*,[30] and extreme gradient boosting trees (XGBoost[31]) approaches.

To avoid overfitting, for each algorithm we employed sample splitting, randomly selecting 80% of the cohort for the training set (i.e., the part of the overall sample used to train the models), with the remainder allocated to the test set (i.e., the part of the overall sample in which the results we present are calculated). To address data missing in the clinical record, we used multiple imputation by chained equations,[32] fitting 10 imputation datasets. Results from different datasets were pooled using Rubin's Rules.[33]

GRF, X-learner, and DR-learner algorithms all have variable importance metrics which can aid in understanding what factors, if any, contribute to heterogeneity in associations between food insecurity and study outcomes. GRF and X-learner report variable importance

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

metrics on a similar scale, while the scale for DR-learner is different. This makes direct numeric comparison between all three methods challenging, but the ranking of the variables, a relative metric of importance, can facilitate such comparisons. Overall, if the methods produce relatively similar rankings for individual variables, it would be interpreted as evidence of consistency of the association between the variable and heterogeneity in outcomes. Or if the methods do not rank variables consistently, it may indicate lack of strong associations between the variable and outcome heterogeneity, with chance variation playing a larger role.

Analyses were conducted in R version 4.2.1 and Python 3.9.13, including use of R packages *mice, grf, ranger, tidyhte,* and Python package *causalml.*[30,34-37]

Results

The dataset used to evaluate the HbA1c outcome included 41,581 individuals (Table 1). The mean age was 56.2 (SD: 12.8) years, 56.9% were female, and mean income expressed as a percentage of the Federal Poverty Guideline was 135% (SD: 321%). Demographics were similar in the datasets used in SBP, DBP, and LDL analyses (eTables 1-3). Mean HbA1c at the time of food insecurity assessment (“baseline”) was 7.8% (SD: 1.9%) and 10,399 participants (25.0%) reported food insecurity. Baseline mean SBP was 129.2 (12.9) mm Hg, mean DBP was 77.8 (7.7) mm Hg, and mean LDL was 100.8 (34.6) mg/dL.

At 12 months, mean HbA1c was 7.6% (SD: 1.9%), mean SBP was 128.5 mm Hg (SD: 14.9 mm Hg), mean DBP was 76.9 mm Hg (SD: 9.0 mm Hg), and mean LDL was 96.8 mg/dL (37.8 mg/dL).

In GRF analyses, having food insecurity was associated with a greater estimated mean HbA1c at 12 months (0.078%, 95%CI 0.031 to 0.124) with only modest heterogeneity in the estimates (Table 2 and Figure 1). For example, the quartile with the lowest estimated difference between having and not having food insecurity had mean difference in HbA1c of 0.0%, while the quartile with the greatest estimated difference had a mean difference in HbA1c of 0.2%.

Results from X-learner and DR-learner followed a similar pattern. For X-learner, the estimated mean difference in HbA1c was 0.084 (95%CI 0.008 to 0.159) greater with food insecurity, again showing modest heterogeneity (lowest quartile mean −0.1%, highest quartile mean 0.2%). For DR-learner, the estimated mean difference in HbA1c was 0.123% (95%CI 0.075 to 0.170) greater with food insecurity, again with modest heterogeneity (lowest quartile mean 0.0%, highest quartile mean 0.3%).

In examining the quartiles with the greatest and least estimated difference, across all three estimation approaches the quartile with the greatest estimated difference had higher baseline HbA1c than average, greater comorbidity burden than average, and a greater prevalence of lacking health insurance than average. The variable importance estimates for GRF and X-learner both ranked baseline HbA1c, SVI, and income as the three most important variables for explaining heterogeneity in estimates (Table 3). DR-learner, which uses a different method for estimating variable importance, ranked these variables lower, meaning

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

there is variability in how the different approaches rank variables. Overall, GRF estimated less variability in outcomes than other methods.

Results for the SBP, DBP, and LDL analyses followed similar patterns (eTables 4-9 and eFigures 1-3). Food insecurity was associated with greater SBP and DBP on average, and there was little heterogeneity. Food insecurity was not associated with greater LDL on average, and there was again little heterogeneity. Further, variable importance rankings were not consistent across methods.

Sensitivity analyses including BMI as a covariate were not meaningfully different from the main analyses (eTable 10).

Discussion

This observational study of adults with T2DM seen in community-based health centers found associations of modest magnitude between food insecurity and the outcomes of HbA1c and blood pressure. These associations did not exhibit meaningful of heterogeneity; most estimates were within a narrow range. Moreover, there was variability in rankings of variable importance across methods, meaning no particular variables were consistently associated with more heterogeneity. No clear association was found between food insecurity and LDL cholesterol on average, again with little heterogeneity and inconsistent variable importance rankings.

These findings expand on those of prior studies. Past observational studies found association between food insecurity and worse diabetes outcomes, as seen here for HbA1c and blood pressure.[5,11] However, some randomized trials of interventions to address food insecurity did not find statistically significant benefits, producing confidence intervals that contain the modest estimates found here.[9,10] This study adds an investigation of heterogeneity of these associations using modern machine learning methods that evaluate multiple combinations of factors simultaneously and are sensitive to possible nonlinearities. One possibility for the relatively modest association seen between food insecurity and study outcomes in this study is that participants did not experience food insecurity for a sufficient duration to see more harmful impacts. However, a prior study with a longer follow-up period did not find that associations between food insecurity diabetes outcomes increased with longer exposure to food insecurity.[11]

These findings have several implications. First, because there seems to be limited heterogeneity in the association between food insecurity and study outcomes, food insecurity interventions may be a case where seeking to identify those most likely to benefit and targeting an intervention only to them is not needed. This may make intervention implementation more convenient. Second, because rankings of variable importance varied across methods, it may be wise to use several methods when trying to understand potential heterogeneity, to avoid possibly being misinformed by the results of any particular method.

One direction for future research would be to examine the possibility of heterogenous treatment effects in actual interventions, rather than in hypothetical scenarios such as these. Though methodological advances have increased our technical ability to do this, sample

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

size requirements are such that it may take relatively large datasets to detect meaningful differences, and trials that are adequately powered to detect average treatment effects may not be powered to detect heterogenous treatment effects.

Results interpretation should consider several limitations. First, in this observational study, associations between food insecurity and T2DM outcomes may not be equivalent to changes in outcomes were food insecurity to be resolved by an actual intervention. Moreover, given the possibility of unmeasured confounding, we do not advocate a causal interpretation of these findings. For example, we did not have data on nutritional status at baseline or smoking status. Finally, study data came from electronic health records so may be subject to measurement error, and data from patients seen in community-based health centers may not be generalizable to all clinical populations. However, these limitations are balanced by several strengths. First, the measures of association between food insecurity and study outcomes were within the confidence limits of effect estimates from prior randomized trials of food insecurity interventions[9,10], lending credibility to the estimates of this study. Second, this study used several advanced methods for detecting HTEs, and a large dataset from across the country, with adequate sample size for even relatively low prevalence features.

In this observational study of the heterogeneity of the associations between food insecurity and T2DM outcomes, food insecurity was associated with worse HbA1c and blood pressure outcomes with relatively little heterogeneity, and was not associated with LDL, again with little heterogeneity. These findings may be useful in planning and understanding the results of food insecurity interventions.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements:

We wish to thank Suzanne Morrissey for project administration. She was compensated through grant R01DK125406 for her efforts.

Funding:

This work was funded in part by R01DK125406. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health. SB was supported by the National Institutes of Health (Grant Nos. 2P30 DK092924 and R01DK116852) and the Centers for Disease Control and Prevention (Grant No. U18DP006526). The research reported in this work was powered by PCORnet®. PCORnet® has been developed with funding from the Patient-Centered Outcomes Research Institute® (PCORI®) and conducted with the Accelerating Data Value Across a National Community Health Center Network (ADVANCE) Clinical Research Network (CRN). ADVANCE is a Clinical Research Network in PCORnet® led by OCHIN in partnership with Health Choice Network, Fenway Health, University of Washington, and Oregon Health & Science University. ADVANCE's participation in PCORnet® is funded through the PCORI Award RI-OCHIN-01-MC.

Role of the Funder:

The funding organizations had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Competing Interests:

SAB reports research grants from NIH, North Carolina Department of Health and Human Services, Blue Cross Blue Shield of North Carolina, Feeding America, the American Diabetes Association, and the American Heart Association, and personal fees from the Aspen Institute, Rockefeller Foundation, Gretchen Swanson Center for Nutrition, and Kaiser Permanente, outside of the submitted work. ML reports research grant support from North Carolina Department of Health and Human Services. All other authors declare nothing to report.

Data Availability:

No additional data available, the terms of our data use agreement do not permit data sharing.

References

1. Rabbitt MP, Reed-Jones M, Hales LJ, Burke MP. Household Food Security in the United States in 2023. Accessed October 3, 2024. http://www.ers.usda.gov/publications/pub-details/?pubid=109895
2. Gundersen C, Ziliak JP. Food Insecurity And Health Outcomes. Health Aff Proj Hope. 2015;34(11):1830–1839. doi:10.1377/hlthaff.2015.0645
3. Volpp KG, Berkowitz SA, Sharma SV, et al. Food Is Medicine: A Presidential Advisory From the American Heart Association. Circulation. 2023;148(18):1417–1439. doi:10.1161/CIR.0000000000001182 [PubMed: 37767686]
4. Brandt EJ, Mozaffarian D, Leung CW, Berkowitz SA, Murthy VL. Diet and Food and Nutrition Insecurity and Cardiometabolic Disease. Circ Res. 2023;132(12):1692–1706. doi:10.1161/CIRCRESAHA.123.322065 [PubMed: 37289902]
5. Berkowitz SA, Meigs JB, DeWalt D, et al. Material need insecurities, control of diabetes mellitus, and use of health care resources: results of the Measuring Economic Insecurity in Diabetes study. JAMA Intern Med. 2015;175(2):257–265. doi:10.1001/jamainternmed.2014.6888 [PubMed: 25545780]
6. Hill-Briggs F, Adler NE, Berkowitz SA, et al. Social Determinants of Health and Diabetes: A Scientific Review. Diabetes Care. Published online November 2, 2020:dci200053. doi:10.2337/dci20-0053 [PubMed: 33139407]
7. Te Vazquez J, Feng SN, Orr CJ, Berkowitz SA. Food Insecurity and Cardiometabolic Conditions: a Review of Recent Research. Curr Nutr Rep. Published online June 21, 2021. doi:10.1007/s13668-021-00364-2
8. Palakshappa D, Ip EH, Berkowitz SA, et al. Pathways by Which Food Insecurity Is Associated With Atherosclerotic Cardiovascular Disease Risk. J Am Heart Assoc. 2021;10(22):e021901. doi:10.1161/JAHA.121.021901 [PubMed: 34743567]
9. Seligman HK, Smith M, Rosenmoss S, Marshall MB, Waxman E. Comprehensive Diabetes Self-Management Support From Food Banks: A Randomized Controlled Trial. Am J Public Health. Published online July 19, 2018:e1–e8. doi:10.2105/AJPH.2018.304528
10. Doyle J, Alsan M, Skelley N, Lu Y, Cawley J. Effect of an Intensive Food-as-Medicine Program on Health and Health Care Use: A Randomized Clinical Trial. JAMA Intern Med. Published online December 26, 2023:e236670. doi:10.1001/jamainternmed.2023.6670
11. Berkowitz SA, Ochoa A, Donovan JM, et al. Estimating the impact of addressing food needs on diabetes outcomes. SSM - Popul Health. 2024;27:101709. doi:10.1016/j.ssmph.2024.101709 [PubMed: 39296549]
12. Hayward RA, Kent DM, Vijan S, Hofer TP. Multivariable risk prediction can greatly enhance the statistical power of clinical trial subgroup analysis. BMC Med Res Methodol. 2006;6:18. doi:10.1186/1471-2288-6-18 [PubMed: 16613605]
13. VanderWeele TJ, Knol MJ. Interpretation of subgroup analyses in randomized trials: heterogeneity versus secondary interventions. Ann Intern Med. 2011;154(10):680–683. doi:10.7326/0003-4819-154-10-201105170-00008 [PubMed: 21576536]
14. Wallach JD, Sullivan PG, Trepanowski JF, Sainani KL, Steyerberg EW, Ioannidis JPA. Evaluation of Evidence of Statistical Support and Corroboration of Subgroup Claims in Randomized

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Clinical Trials. JAMA Intern Med. 2017;177(4):554–560. doi:10.1001/jamainternmed.2016.9125 [PubMed: 28192563]

15. Basu S, Johnson KT, Berkowitz SA. Use of Machine Learning Approaches in Clinical Epidemiological Research of Diabetes. Curr Diab Rep. 2020;20(12):80. doi:10.1007/s11892-020-01353-5 [PubMed: 33270183]
16. Kennedy EH, Balakrishnan S, Robins JM, Wasserman L. Minimax rates for heterogeneous causal effect estimation. Published online February 8, 2023. Accessed February 10, 2023. http://arxiv.org/abs/2203.00837
17. Künzel SR, Sekhon JS, Bickel PJ, Yu B. Metalearners for estimating heterogeneous treatment effects using machine learning. Proc Natl Acad Sci U S A. 2019;116(10):4156–4165. doi:10.1073/pnas.1804597116 [PubMed: 30770453]
18. Inoue K, Athey S, Baicker K, Tsugawa Y. Heterogeneous effects of Medicaid coverage on cardiovascular risk factors: secondary analysis of randomized controlled trial. BMJ. 2024;386:e079377. doi:10.1136/bmj-2024-079377 [PubMed: 39313257]
19. Gold R, DeVoe JE, McIntire PJ, Puro JE, Chauvie SL, Shah AR. Receipt of diabetes preventive care among safety net patients associated with differing levels of insurance coverage. J Am Board Fam Med JABFM. 2012;25(1):42–49. doi:10.3122/jabfm.2012.01.110142 [PubMed: 22218623]
20. Gold R, Cottrell E, Bunce A, et al. Developing Electronic Health Record (EHR) Strategies Related to Health Center Patients' Social Determinants of Health. J Am Board Fam Med. 2017;30(4):428–447. doi:10.3122/jabfm.2017.04.170046 [PubMed: 28720625]
21. Gold R, Kaufmann J, Gottlieb LM, et al. Cross-Sectional Associations: Social Risks and Diabetes Care Quality, Outcomes. Am J Prev Med. 2022;63(3):392–402. doi:10.1016/j.amepre.2022.03.011 [PubMed: 35523696]
22. PRAPARE. NACHC. Accessed August 20, 2019. http://www.nachc.org/research-and-data/prapare/
23. CMS. The Accountable Health Communities Health-Related Social Needs Screening Tool. Accessed September 28, 2019. https://innovation.cms.gov/Files/worksheets/ahcm-screeningtool.pdf
24. Bickel G, Nord M, Price C, Hamilton W, Cook J. Guide to Measuring Household Food Security, Revised 2000. Published online March 2000. Accessed September 17, 2018. https://fns-prod.azureedge.net/sites/default/files/FSGuide.pdf
25. Sun JW, Rogers JR, Her Q, et al. Adaptation and Validation of the Combined Comorbidity Score for ICD-10-CM. Med Care. 2017;55(12):1046–1051. doi:10.1097/MLR.0000000000000824 [PubMed: 29087983]
26. CDC/ATSDR Social Vulnerability Index (SVI). February 23, 2024. Accessed March 28, 2024. https://www.atsdr.cdc.gov/placeandhealth/svi/index.html
27. Athey S, Tibshirani J, Wager S. Generalized Random Forests. Published online April 5, 2018. doi:10.48550/arXiv.1610.01271
28. Kennedy EH. Towards optimal doubly robust estimation of heterogeneous causal effects. Published online August 21, 2023. doi:10.48550/arXiv.2004.14497
29. van der Laan MJ, Polley EC, Hubbard AE. Super learner. Stat Appl Genet Mol Biol. 2007;6:Article25. doi:10.2202/1544-6115.1309
30. Wright MN, Ziegler A. ranger: A Fast Implementation of Random Forests for High Dimensional Data in C++ and R. J Stat Softw. 2017;77:1–17. doi:10.18637/jss.v077.i01
31. Chen T, Guestrin C. XGBoost: A Scalable Tree Boosting System. In: Proceedings of the 22nd ACM SIGKDD International Conference on Knowledge Discovery and Data Mining. ; 2016:785–794. doi:10.1145/2939672.2939785
32. Azur MJ, Stuart EA, Frangakis C, Leaf PJ. Multiple imputation by chained equations: what is it and how does it work? Int J Methods Psychiatr Res. 2011;20(1):40–49. doi:10.1002/mpr.329 [PubMed: 21499542]
33. Little DB, Rubin R. Statistical Analysis with Missing Data. 2nd ed. Wiley-Interscience; 2002.
34. van Buuren S, Groothuis-Oudshoorn K, Vink G, et al. mice: Multivariate Imputation by Chained Equations. Published online June 5, 2023. Accessed March 8, 2024. https://cran.r-project.org/web/packages/mice/index.html

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

35. Tibshirani J, Athey S, Friedberg R, et al. grf: Generalized Random Forests. Published online November 15, 2024. Accessed December 13, 2024. https://cran.r-project.org/web/packages/grf/index.html

36. Dimmery D. tidyhte: Tidy Estimation of Heterogeneous Treatment Effects. Published online August 14, 2023. Accessed December 13, 2024. https://cran.r-project.org/web/packages/tidyhte/index.html

37. uber/causalml. Published online December 13, 2024. Accessed December13, 2024. https://github.com/uber/causalml

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

What is already known on this topic:

Food insecurity is associated with worse diabetes outcomes, but how those associations may vary across individuals is not well studied.

What this study adds:

There was little heterogeneity in the associations between food insecurity and diabetes outcomes.

How this study might affect research, practice or policy:

Because there is little heterogeneity in the associations between food insecurity and diabetes outcomes, targeting of food insecurity interventions may not be needed.

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

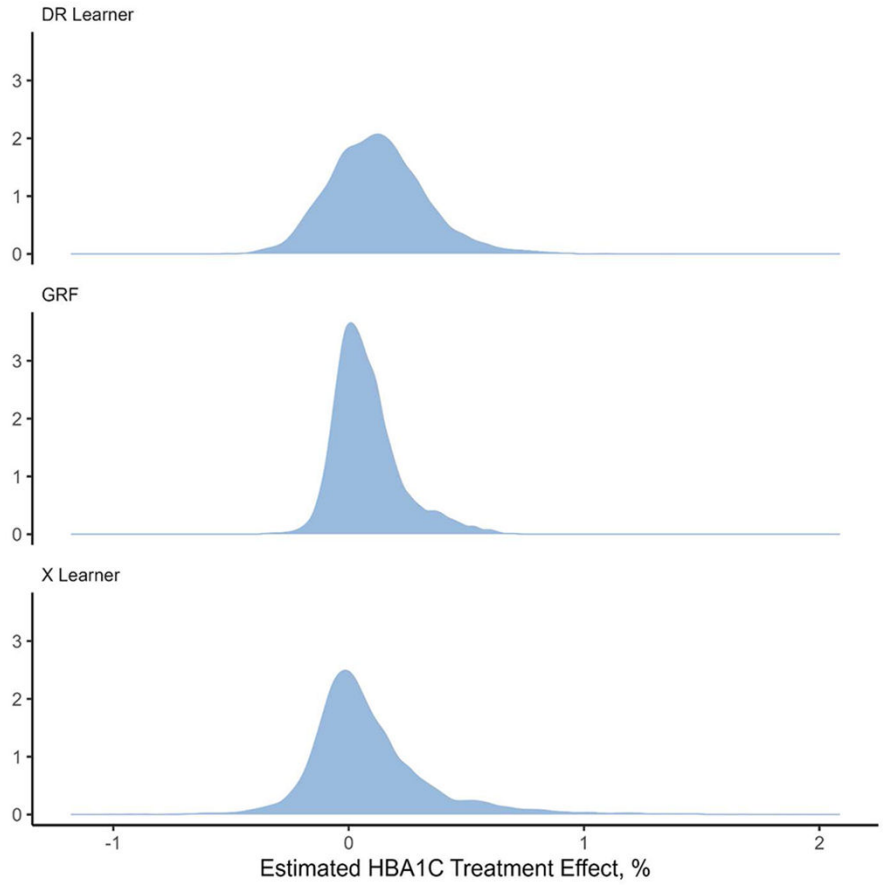


Figure 1:

Density plot of estimated differences in HbA1c

Density plot depicts the distribution of estimates comparing counterfactual scenarios in which individuals did vs. did not experience food insecurity, with an outcome of HbA1c at 12 months after food insecurity assessment. Three different estimation approaches are used: DR-learner, GRF, and X-learner. The y-axis indicates the density of estimates and the x-axis indicates the estimated difference between the two counterfactual scenarios (an estimate of the 'treatment effect' of resolving food insecurity on the outcome).

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Table 1:

Demographics of Overall Cohort for HbA1c Analyses

	Overall	**Food Insecurity = 0**	**Food Insecurity = 1**
	N = 41581	**N = 31182**	**N = 10399**
	Mean or N (SD or %)	**Mean or N (SD or %)**	**Mean or N (SD or %)**
Age	56.2 (12.8)	56.9 (13.1)	54.3 (11.6)
Age Missing	0 (0)	0 (0)	0 (0)
Gender			
Male	17918 (43.1)	13618 (43.7)	4300 (41.4)
Female	23651 (56.9)	17557 (56.3)	6094 (58.6)
Missing	12 (0)	7 (0)	5 (0)
Race			
Black	11259 (27.1)	8377 (26.9)	2882 (27.7)
White	24433 (58.8)	18433 (59.1)	6000 (57.7)
Other	2707 (6.5)	2184 (7)	523 (5)
Missing	3182 (7.7)	2188 (7)	994 (9.6)
Ethnicity			
Hispanic	14031 (33.7)	10581 (33.9)	3450 (33.2)
Non-Hispanic	26381 (63.4)	19739 (63.3)	6642 (63.9)
Missing	1169 (2.8)	862 (2.8)	307 (3)
Insurance			
Medicaid	14217 (34.2)	9838 (31.6)	4379 (42.1)
Medicare	11192 (26.9)	8825 (28.3)	2367 (22.8)
Private	7634 (18.4)	6329 (20.3)	1305 (12.6)
Uninsured	7872 (18.9)	5678 (18.2)	2194 (21.1)
Missing	666 (1.6)	512 (1.6)	154 (1.5)
Income	134.5 (320.8)	145.3 (345.4)	103.9 (235.4)
Income Missing	6901 (16.6)	5585 (17.9)	1316 (12.7)
SVI	0.7 (0.2)	0.7 (0.2)	0.7 (0.2)
SVI Missing	7640 (18.4)	5988 (19.2)	1652 (15.9)
Comorbidity Index	0.2 (0.9)	0.2 (0.9)	0.3 (0.9)
Comorbidity Index Missing	322 (0.8)	250 (0.8)	72 (0.7)
Baseline HbA1c	7.8 (1.9)	7.7 (1.8)	7.9 (2)
Baseline HbA1c Missing	11290 (27.2)	8888 (28.5)	2402 (23.1)
12 Month HbA1c	7.6 (1.9)	7.6 (1.9)	7.8 (2.1)

HbA1c = Hemoglobin A1c

SVI = social vulnerability index

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Table 2:

Demographics of Test Data Set, Overall and by Quartile of Estimated HbA1c Difference

		GRF		X-Learner		DR-Learner	
	Overall	**Quartile with Greatest Estimated Difference in HbA1c**	**Quartile with Lowest Estimated Difference in HbA1c**	**Quartile with Greatest Estimated Difference in HbA1c**	**Quartile with Lowest Estimated Difference in HbA1**	**Quartile with Greatest Estimated Difference in HbA1c**	**Quartile with Lowest Estimated Difference in HbA1**
	N = 8317	**N = 2080**	**N = 2080**	**N = 2080**	**N = 2080**	**N = 2080**	**N = 2080**
	Mean or N (SD or %)	**Mean or N (SD or %)**	**Mean or N (SD or %)**	**Mean or N (SD or %)**	**Mean or N (SD or %)**	**Mean or N (SD or %)**	**Mean or N (SD or %)**
Estimated Difference in Outcome	--	0.2	0.0	0.2	−0.1	0.3	0.0
Age	56.1 (12.7)	53.2 (12.4)	57.7 (12.1)	53.2 (13.0)	56.0 (13.6)	51.4 (13.0)	59.9 (11.7)
Gender							
Male	3553 (42.7)	1003 (48.2)	860 (41.3)	979 (47.1)	934 (44.9)	1092 (52.5)	647 (31.1)
Female	4764 (57.3)	1077 (51.8)	1220 (58.7)	1101 (52.9)	1147 (55.1)	989 (47.5)	1433 (68.9)
Race							
Black	2433 (29.2)	583 (28.0)	694 (33.4)	591 (28.4)	668 (32.1)	249 (12.0)	1201 (57.7)
White	5319 (64.0)	1377 (66.2)	1243 (59.7)	1377 (66.2)	1263 (60.7)	1729 (83.1)	708 (34.1)
Other Categorization	565 (6.8)	120 (5.8)	143 (6.9)	112 (5.4)	149 (7.1)	102 (4.9)	171 (8.2)
Ethnicity							
Hispanic	2890 (34.7)	750 (36.1)	763 (36.7)	713 (34.3)	814 (39.1)	1164 (55.9)	297 (14.3)
Non-Hispanic	5427 (65.3)	1330 (63.9)	1318 (63.3)	1368 (65.7)	1266 (60.9)	917 (44.1)	1783 (85.7)
Insurance							
Medicaid	2895 (34.8)	686 (33.0)	768 (36.9)	656 (31.5)	812 (39.0)	770 (37.0)	607 (29.2)
Medicare	2217 (26.7)	404 (19.4)	623 (30.0)	475 (22.8)	511 (24.6)	461 (22.2)	594 (28.6)
Private	1572 (18.9)	434 (20.8)	375 (18.0)	438 (21.1)	385 (18.5)	259 (12.4)	584 (28.1)
Uninsured	1633 (19.6)	556 (26.7)	314 (15.1)	512 (24.6)	372 (17.9)	590 (28.4)	295 (14.2)
Income	135 (323.3)	128 (286.0)	114 (325.3)	143 (303.5)	155 (422.4)	121 (330.6)	161 (360.1)
SVI	0.70 (0.24)	0.65 (0.26)	0.75 (0.20)	0.65 (0.27)	0.72 (0.24)	0.76 (0.21)	0.62 (0.27)
Comorbidity Index	0.2 (0.9)	0.4 (0.9)	0.1 (0.8)	0.4 (1.0)	0.1 (0.9)	0.4 (0.9)	0.0 (0.9)
Baseline HbA1c	7.7 (1.9)	9.9 (1.8)	6.4 (0.9)	9.0 (2.1)	7.2 (1.9)	9.6 (2.1)	6.6 (1.0)

This table presents demographic characteristics of individuals in the quartile estimated to have the greatest difference in hemoglobin a1c values if they did vs. did not experience food insecurity, and the characteristics of individuals in the quartile estimated to have the lowest difference in hemoglobin a1c values if they did vs. did not experience food insecurity, organized by the method used to estimate heterogeneity. For example, compared with the overall mean hemoglobin A1c at baseline of 7.7, those estimated to have the greatest difference in hemoglobin a1c under the counterfactual scenarios of experiencing vs. not experiencing food insecurity had mean hemoglobin a1c of 9.9 (when using the GRF method), 9.0 (when using the X-Learner method) and 9.6 (when using the DR-Learner method). Taken together, this suggests that food insecurity may more strongly impact the hemoglobin a1c of those with greater baseline hemoglobin a1c. However, it is important to keep in mind that the magnitude of the difference across quartiles is relatively modest.

GRF: Generalized random forest

DR-Learner: Doubly Robust learner

HbA1c = Hemoglobin A1c

SVI = social vulnerability index

Author Manuscript
Author Manuscript
Author Manuscript
Author Manuscript

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Table 3:

Variable Importance Metrics for HbA1c Analyses

GRF		X-learner		DR-learner	
Variable	**Value**	**Variable**	**Value**	**Variable**	**Value**
Baseline HbA1c	0.675	Baseline HbA1c	0.387	Medicare Insurance	0.0018
SVI	0.120	SVI	0.225	Female	0.0017
Income	0.069	Income	0.134	Comorbidity	0.0016
Age	0.066	Age	0.119	White	0.0014
Comorbidity	0.027	Comorbidity	0.040	Baseline HbA1c	0.0012
Medicaid Insurance	0.012	Medicaid Insurance	0.027	Hispanic	0.0009
Uninsured	0.008	Female	0.023	SVI	0.0008
Hispanic	0.007	Uninsured	0.013	Age	0.0007
Female	0.006	Black	0.010	Black	0.0007
Black	0.004	Hispanic	0.009	Medicaid Insurance	0.0007
White	0.004	Medicare Insurance	0.007	Uninsured	0.0005
Medicare Insurance	0.002	White	0.006	Income	0.0004

SVI = social vulnerability index

GRF and X-learner use similar variable importance metrics so the variable importance values are directly comparable. DR-learner uses a different metric so numeric values are difficult to compare with other methods, but rankings can be compared