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Personalized predictions to identify individuals most likely to achieve 10% weight loss with a lifestyle intervention

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Abstract

Objective: The objective of this study is to generate an algorithm for making predictions about individual treatment responses to a lifestyle intervention for weight loss to maximize treatment effectiveness and public health impact.

Methods: Using data from Action for Health in Diabetes (Look AHEAD), a national, multisite clinical trial that ran from 2001 to 2012, and machine-learning techniques, we generated predicted individual treatment effects for each participant. We tested for heterogeneity in treatment response and computed the degree to which treatment effects could be improved by targeting individuals most likely to benefit.

Results: We found significant individual differences in effects of the Look AHEAD intervention. Based on these predictions, two-thirds of the sample was predicted to experience a treatment effect within ±2% weight loss from the average treatment effect. If the treatment was targeted to the 69% of patients expected to meet a 7% weight-loss target at 1-year follow-up, the average treatment effect increases, with 10% average observed weight loss in the intervention group.

Conclusions: The Look AHEAD intervention would achieve a 10% average weight reduction if targeted to those most likely to benefit. Future research must seek external validation of these predictions. We make this algorithm available with instructions for use to demonstrate its potential capacity to inform shared decision-making and patient-centered care.

INTRODUCTION

Overweight and obesity currently affect 40% and 13% of the global population [1], respectively, with an expected doubling of impacts on disability and death by 2030 [2]. Effective treatments are needed to prevent and treat excess weight and its comorbidities, which include diabetes, cardiovascular disease (CVD), cancer, and chronic kidney disease. Ensuring that multiple viable interventions are available facilitates shared decision-making, an approach in which physicians work collaboratively with patients to provide education and to match the values of care-seeking individuals with a chosen treatment [3].

Rapid advances in weight-management drugs such as glucagon-like peptide-1 (GLP-1) receptor agonists have recently made pharmacological interventions viable [4, 5]. These drugs increase insulin and satiety and decrease hunger and cravings, resulting in average declines of up to 17% of initial weight [6]. Although these outcomes are large, drawbacks exist; reversal occurs following medication cessation [7], negative side effects are possible, including pancreatitis, gastroparesis, and bowel obstruction [8]; evidence supporting their

long-term use is lacking; and high treatment costs limit applicability to the global epidemic [9]. In contrast, behavioral weight-loss interventions have proven less effective, with small effect sizes and/or high costs. Meta-analyses of behavioral approaches with a wide range of intensities report mean weight-loss effects of ~2 to 3 kg, with limited benefit to health outcomes [10]. Moderate high-intensity, or high-effort behavioral interventions that include severe dietary restrictions and increased physical activity, are required to achieve average treatment effects of 5% to 10% weight loss in 1 year [11, 12]. However, individual differences in outcomes are large [13]. If behavioral interventions are going to remain a viable option for patients seeking weight loss, efficacy must improve.

This paper proposes that the varied behavioral treatment options, complex genetic and psychosocial etiologies, and the wide range in individual outcomes associated with weight-loss interventions can be leveraged by clinicians and their patients to create maximally effective personalized behavioral treatment plans. Although the 5% weight reduction suggested by public health agencies and professional societies [14] alleviates some risk factors and high prevalence diseases [15], weight loss beyond 5% results in additional benefits for most health outcomes [16]. Furthermore, nonlinear, step function responses from increased weight loss are evident for some diseases, including the reduction of proinflammatory markers and the relief of osteoarthritic pain at greater than 10% loss [16, 17]. Finally, the greatest reduction in morbidity and mortality is achieved from a weight loss of 10% or greater [18]. Thus, we, along with leading researchers and funders in the field [19], argue that personalized approaches to behavioral interventions should be used to guide clinicians and their patients to treatments that achieve this higher weight reduction. Through personalized approaches, behavioral interventions can provide a viable, safe, and accessible alternative to pharmacological interventions.

The goal of personalized medicine and this study is to predict heterogeneous, individual patient responses to an array of treatment options to facilitate optimal treatment decisions. The current study begins this process with data from the Action for Health in Diabetes (Look AHEAD) lifestyle intervention, an a priori selected set of baseline covariates, and the predicted individual treatment effect (PITE) approach [20] to estimate an algorithm that provides personalized predictions of treatment effects. We aim to do the following 1) test for significant individual differences in the Look AHEAD lifestyle intervention on weight loss; 2) describe the range of predicted individual differences for the full sample, as well as predictive intervals for these differences; and 3) quantify the degree to which weight loss could have been increased by using these predictions to recommend treatment to those most likely to benefit. The algorithm is made available with an example, illustrating how predictions of response to the intervention and a predictive interval can be obtained for any individual with data for the covariates used to derive the algorithm. Our goal is to show the outcomes possible when using individual predictions to help select treatment options.

Study Importance

What is already known?

- A 10% average weight loss in 1 year is required to actualize numerous positive health impacts.
- Trials have shown that lifestyle interventions often result in modest weight loss, but substantial heterogeneity exists in treatment response.
- Personalized medicine can help to identify the likelihood of a sufficiently positive outcome for a given patient.

What does this study add?

- The current study demonstrates the feasibility of a priori identification of patients likely to achieve clinically meaningful weight loss through a lifestyle intervention for obesity.
- This study developed and has made available an algorithm that, after external validation, could be used in a clinical setting to obtain predictions for out-of-sample patients.

How might these results change the direction of research or the focus of clinical practice?

- Pharmacological approaches promise large effect sizes but are not widely accessible to all who need treatment. Intensive lifestyle interventions still provide the most accessible option for the treatment of obesity and type 2 diabetes.
- Lifestyle interventions are time- and resource-intensive. Personalized medicine for obesity can increase patient choice beyond pharmacological or surgical options while achieving meaningful weight reduction for many patients and improving efficiency of resource expenditure.

METHODS

Personalized medicine methods

In the past decade, new methods for personalized medicine have emerged. Many use predictive models (machine learning) and the potential outcomes framework to predict treatment responses for individuals or groups as a function of the combined effects of many baseline predictors [21]. These methods focus on obtaining replicable predictions rather than identifying mechanisms for treatment effects [22], thereby producing results that have direct implications for clinical practice. A previous study classified patients into four phenotypes, which were then used to guide the choice of obesity medication, greatly improving weight loss [23]. Another study used the same

approach used here to show that a school-based preventive intervention impacted body mass index (BMI) *z* score for some students more meaningfully than others [24]. This is the first study, of which we are aware, to examine whether a widely available weight-loss intervention shows clinically meaningful differences in treatment effects and to evaluate future improvement of clinical outcomes among patients with type 2 diabetes by using data to target treatments. This approach could be adapted and implemented in routine clinical practice to develop personalized treatment plans based on an individual's predicted response to behavioral and pharmacological interventions.

Look AHEAD trial

This study uses data from the Look AHEAD trial (ClinicalTrials.gov NCT00017953) [25] to develop a predictive algorithm that captures individual differences in the effects of the lifestyle intervention. Participants were recruited at 16 clinical centers across the United States beginning in 2001. Initial follow-up occurred 1 year after randomization. Participants were eligible if they were between the ages of 45 and 74 years, had BMI ≥ 25 kg/m^2 (or ≥27 kg/m^2 if they were currently taking insulin), and had been diagnosed with type 2 diabetes mellitus. The final sample of the original trial included 5145 individuals with overweight or obesity and type 2 diabetes. Participants were randomized to lifestyle intervention (the intervention group) or diabetes support and education (the control group). Our final sample included 4526 individuals who had complete data for the 23 variables used in the predictive algorithm.

The primary outcome of Look AHEAD was time to incidence of major CVD event. Increase in time to event was expected to be achieved primarily through an average of at least 7% weight loss in response to the intensive lifestyle intervention compared to control. In addition to targeting weight loss, the intensive lifestyle intervention also sought to increase cardiorespiratory fitness to increase time to event. The study successfully achieved the targeted weight loss [12], but there was not a significant reduction in heart-related events. The lifestyle intervention implemented in Look AHEAD closely followed an earlier intervention from the Diabetes Prevention Study (DPP) [26], which elicited an average 7% reduction in weight. The Look AHEAD intervention remains in widespread use for weight loss; therefore, the ability to predict which patients will best respond to the intervention has the potential to improve shared decision-making (i.e., collaborative discussions between health care providers and patients to make the best health care decision for the patient).

Look AHEAD intervention

The intervention (see reference for detailed description) included 24 group and individual sessions in the first 6 months and 18 sessions in the second 6 months [27]. The sessions included both diet and physical activity components with previous evidence for efficacy [28]. Group sessions focused on behavioral weight control (e.g., recording food intake, coping with negative thoughts about eating), and participants were weighed and reported on their calorie intake and their success at meeting their goals. In once-a-month individual sessions, lifestyle counselors tailored treatment to participants' needs. Participants were encouraged to replace two meals and one snack per day with liquid shakes or meal bars. Advanced toolkits were introduced after 6 months for participants who had not lost at least 5% or had regained 2% or more of their body weight. These additional treatment components consisted of prepackaged meals, cooking classes, a gym membership, exercise equipment, or medication. Only one medication was prescribed in the study (orlistat), and its use was discontinued due to limited effectiveness [27].

Diabetes support and education

The active control condition consisted of three 1-h informational group sessions that covered topics related to diet, physical activity, and social support. Participants were not provided with specific behavioral strategies and were told to contact their primary care providers for more help losing weight [12].

Outcome

A primary target in Look AHEAD was a 7% reduction in weight in 1 year [27]. Therefore, in this study, we use percent reduction in weight as the primary outcome.

Baseline predictors of individual differences

One of the most important decisions in predictive models is determining which predictors to include in the analysis. Prior to analysis, covariates for the PITE algorithm were selected by three coauthors (i.e., Elizabeth Y. Jimenez, Dawn K. Wilson, and Ken Resnicow), each of whom has extensive experience with interventions to treat and prevent obesity. Because PITEs combine the joint effects of baseline predictors into one prediction in which no individual variable is distinguished, it is important to carefully select the covariates that are most likely to predict heterogeneity in treatment effect based on theory, prior empirical findings, and clinical experience [29,30]. Limiting the number of predictors used to those most likely to drive heterogeneity in treatment response leads to more efficient predictions because the addition of unneeded covariates to the predictive model introduces greater noise to PITE estimates and power for the permutation test is reduced [31]. The Look AHEAD baseline covariates with less than 3% missing data were presented to the team. Members reached a consensus on the variables that previous evidence, theory, or experience suggested could predict differential treatment effects. The selected baseline predictors are described in Table 1.

Data analysis

We used the PITE approach (detailed elsewhere [20,24]) to derive an algorithm to calculate personalized predictions of the effects of the

TABLE 1 Baseline predictors of individual heterogeneity in response to the Look AHEAD intervention.

Baseline predictors	Description	Range	Mean/proportion
Sex	0 = male; 1 = female	(0, 1)	0.58
Race and ethnicity	White (ref), Black, Hispanic, other	(0, 1)	0.16 (Black) 0.14 (Hispanic) 0.04 (other)
Age, y		(44, 76)	59.0
Education	Less than HS, HS/GED, AA/Voc, some college (ref), Bachelor's, Master's/some grad school, doctorate (e.g., MD, PhD, JD)	(0, 1)	0.06 (<HS) 0.13 (HS) 0.14 (AA/Voc) 0.22 (Bachelor') 0.15 (Master's) 0.05 (MD/PhD/JD)
Weight, kg	Average of 2 weight measurements, kg	(58, 182.7)	101.14
Employment status	0 = employed or not searching for a job; 1 = unemployed/laid off	(0, 1)	0.21
Marital status	Never married, married/partnered (ref), divorced/separated, or widowed	(0, 1)	0.07 (Never married) 0.18 (Divorced) 0.07 (Widowed)
Smoking status	Current smoking, past smoking, or never smoked (ref)	(0, 1)	0.04 (Current) 0.46 (Past)
Alcohol consumption, oz/wk	Sum oz/wk consumed of beer, wine, and liquor	(0, 864)	8.75
Binge eating	Eaten a large amount of food in 2 h or less and felt that they could not control what or how much they were eating	(0, 1)	0.35
ABI [37]	Average of 2 measurements of ABI	(0.6, 2.7)	1.16
Hemoglobin A1C	Hemoglobin A1C %	(4.7, 14.5)	7.26
Maximum MET [38]	Maximum MET during graded exercise test	(3.3, 16.7)	7.21
Family history of diabetes	Family member has diabetes	(0, 1)	0.64
Medical history of CVD	Diagnosed with CVD	[0, 1]	0.14
Framingham Risk Score [39]	Coronary heart disease event risk in 1 y	(0, 0.13)	0.02
Metabolic syndrome	Number of metabolic syndrome criteria met	(1, 5)	3.92
SF-36 general health score [40]	Summed score of multiitem scales: physical functioning, role limitations due to physical health problems, bodily pain, general health perceptions, vitality, social functioning, role limitations due to emotional problems, and mental health	(16.2, 63.9)	47.24
BDI [41]	BDI score; excludes item regarding weight	(0, 35)	5.35
Taking diabetes medication	No/yes	(0, 1)	0.88
Taking antihypertension medication	No/yes	(0, 1)	0.75
Taking insulin	No/yes	(0, 1)	0.18
Taking lipid-lowering medication	No/yes	(0, 1)	0.52

Abbreviations: ABI, ankle brachial index; AA, associate of arts degree; BDI, Beck Depression Inventory; CVD, cardiovascular disease; GED, general quivalency diploma; HS, high school degree; Look AHEAD, Action for Health in Diabetes; MET, metabolic equivalent of task; ref, reference; SF-36, 36-Item Short Form Survey; Voc, vocational degree.

Look AHEAD lifestyle intervention on weight loss. The algorithm [32] is as follows:

1. Train a predictive model for the outcome for those in the control condition $\left(Y_i^c = f_c(x_i) + \varepsilon_{ic}\right)$.
2. Train a predictive model for those in treatment $\left(Y_i^t = f_t(x_i) + \varepsilon_{it}\right)$.
3. Compute the predicted value under control, $\widehat{Y}_i^c$, and under treatment, $\widehat{Y}_i^t$, for an individual using his or her values on baseline covariates.
4. Estimate the individual's PITE as the difference in these two predicted values $\left(\widehat{\text{PITE}}_i = \widehat{Y}_i^t - \widehat{Y}_i^c\right)$.

This approach estimates a predictive algorithm for the outcome using selected baseline covariates (x_i) separately for those in the treatment and control conditions. Separating the conditions at this stage allows for the estimation of predicted effects for each individual for both treatment and control conditions. The PITE for any individual is calculated as the difference between the predicted outcome under treatment $(\widehat{Y}_i^t)$ and the predicted outcome under control $(\widehat{Y}_i^c)$. Herein, Bayesian additive regression trees and 23 baseline covariates were used to generate predictions [33]. Due to the large sample in the Look AHEAD trial and the relatively small proportion of missing data concentrated in a few individual cases lost to follow-up (7.9%), we accounted for missing data using listwise deletion.

We used a permutation test to evaluate whether there were significant individual differences in the Look AHEAD intervention's effect on weight loss [27]. This tested whether the SD of the PITEs was larger than could be expected due to chance. Next, we calculated predictive intervals for each individual using quantiles from the Bayesian posterior estimates [34]. These intervals illustrate the expected range of the individual treatment effect. For example, if the interval includes zero, it is not clear that the lifestyle intervention is more effective than the standard of care (control condition) for that individual. Importantly, whereas clinical trial data are used to generate the algorithm, predictions can then be obtained for any individuals for whom all baseline covariates are measured. Therefore, our results can be directly applied to clinical practice.

Data for these analyses were accessed through the National Institute of Diabetes and Digestive and Kidney Diseases and performed in accordance with the terms of the data use agreement with that agency. All analyses were performed in R version 4.3.2 (R Project for Statistical Computing). All individual-level results reported subsequently (descriptions of individual differences, predictive intervals, and increase in treatment efficacy) were obtained using 10-fold cross-validation [35].

RESULTS

Test for the presence of individual differences in the Look AHEAD lifestyle intervention on weight loss

PITEs were calculated for the 4526 individuals in the Look AHEAD trial with complete data using the predictive algorithm based on the 23 baseline covariates selected a priori. A permutation test showed significant individual differences in the effects of the Look AHEAD lifestyle intervention among study participants ($p < 0.001$). The SD of the PITEs was 2.15, indicating that an individual's PITE was predicted to deviate from the average treatment effect by a weight loss of ±2%.

Describe the range and intervals of predicted individual differences in the Look AHEAD lifestyle intervention

To understand the clinical relevance of this heterogeneity, we examined the distribution of the PITEs, as well as their predictive intervals, for each participant. For ease of interpretation, Figure 1 shows individual PITEs and predictive intervals for a simple random sample of 100 individuals and highlights the individual at the 25th and 75th percentiles for the entire dataset. PITEs for the full sample ranged from −0.95 to −15.47, indicating that participants were predicted to lose between 0.95% and 15.47% of their body weight with the intervention versus control. The median PITE was −8.08, meaning that an individual at the 50th percentile of PITEs could be expected to lose ∼8% of his or her weight with the intervention versus control. Although the range of PITEs was substantial, PITEs were fairly normally distributed, and the median PITE reflects the average treatment effect observed of the intensive lifestyle intervention.

In Figure 1, the interval for each individual is defined by the 20th and 80th percentiles for the PITE, representing the range of weight loss expected for that person. Differences in the width of the predictive intervals indicate that, for some individuals, the prediction is more precise than for others. Each line with its center can be obtained for any new patient on whom the 23 baseline covariates are measured.

Could weight loss be maximized by using PITEs to target treatment to those most likely to benefit?

To assess the potential for improving population health using personalized medicine predictions, we identified a "target" group of individuals who were predicted to achieve Look AHEAD's 7% weight-loss target. The target group included 3135 (69.3%) participants. We then assessed the average treatment effect in the target group (Figure 2). The average treatment effect for the target group was a weight loss of 9.6%. Individuals in the treatment condition within the target group lost 10.0% of their body weight. For the 1391 (30.7%) individuals not in the target group, the observed treatment effect was a 4.5% weight loss. Therefore, targeting treatment to the 69.3% of patients, based on selected baseline covariates, was predicted to result in an average doubling of weight loss.

Weight-loss interventions achieve optimal health benefits if a 10% or greater reduction in weight is achieved. We identified a new target group of those whose PITEs indicated that they could expect ≥10% weight loss within the first year (vs. 7% as described earlier) with treatment. This new target group included 864 (19.1%) participants. Treated participants achieved an average treatment effect of 12.9% weight loss compared to participants in the control condition. Therefore, although the number of participants expected to achieve 10% weight loss is modest (19.1% of full sample), the observed average treatment effect for this group (12.9% weight loss) approaches that observed with GLP-1 receptor agonists [6]. In summary, 69% of the sample was expected to reach the target of 7% or greater weight loss, and, on average, the treatment effect for these participants was a 10% weight loss, thereby reaching the weight-loss threshold identified in existing literature as resulting in the greatest reductions in morbidity and mortality. Furthermore, 19% of the sample was predicted to lose 10% or more of their body weight by the 1-year follow-up. For these participants, the average treatment effect was observed to be a 12.9% weight loss.

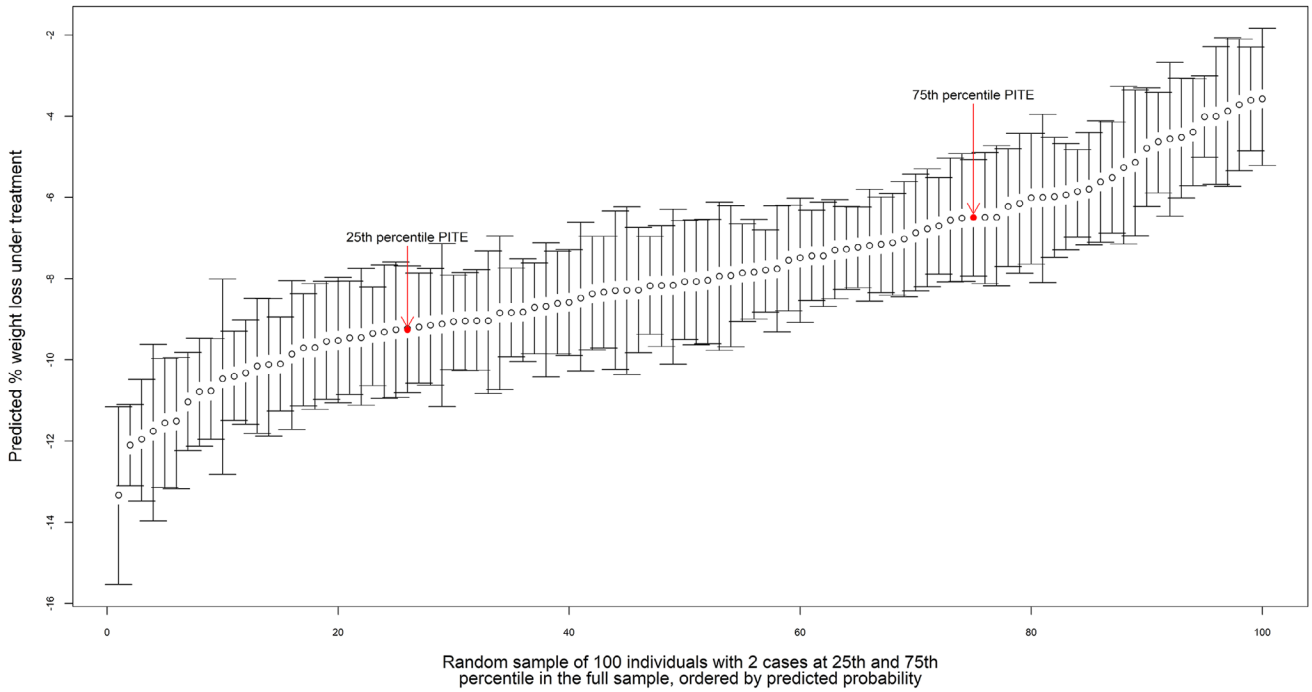

FIGURE 1 Predictive intervals and PITEs for 100 randomly selected Look AHEAD participants. Plot showing PITEs as percentage of loss of body weight (y-axis) for a random sample of 100 individuals (x-axis) from the analytic sample. Individuals were sorted from lowest (greatest predicted weight loss) to highest (least predicted weight loss) PITE. Error bars denote the predictive interval for each individual's PITE. PITEs representing the 25th and 75th percentiles of PITEs for the entire sample are highlighted to show location in the distribution of individuals who are predicted to have 25% greater and 25% less weight loss than the median (8% weight loss). Look AHEAD, Action for Health in Diabetes; PITE, predicted individual treatment effect. [Color figure can be viewed at wileyonlinelibrary.com]

DISCUSSION

This study demonstrates that it may be possible to predict individual responses to a lifestyle-based weight-loss treatment. The goal of personalized medicine is to provide predictions for how individual patients will respond to an array of interventions to allow health care providers and their patients to make optimal treatment decisions together. Rather than being prescriptive, the development of these predictions may serve as a tool to help health care providers and patients determine whether specific lifestyle interventions can assist in meeting weight-loss goals. These results show that it is possible to predict clinically meaningful differences in treatment effectiveness across patients and provide an algorithm for obtaining individual predictions and predictive intervals. Once replicated, these results will achieve the first step in personalized medicine, i.e., providing clinically useful individual predictions for patients for a widely used lifestyle intervention for weight loss.

To fully realize the potential of personalized medicine using these predictions, future research needs to obtain predictions across an array of widely available interventions, replicate these results in independent data, provide a method for obtaining predictions when covariates are missing, and develop an efficient system for obtaining necessary data from patients or from the electronic medical record and providing it to health care providers in a readily accessible format. Although this study represents an initial step, it is critical because it shows that the magnitude of treatment effects (weight loss) can be greatly increased with this approach in future clinical application. Using PITE predictions to target the intervention to the 68% of respondents most likely to achieve desired outcomes would increase the average treatment effects to nearly 10% weight loss, a clinically important threshold to have a population-level impact at reducing morbidity and mortality [18].

In considering application to clinical practice, it is important to keep in mind that the PITE approach incorporates variables such as modifiable lifestyle factors to develop an algorithm. Importantly, the PITE approach cannot identify individual variables within the algorithm as more important than others in determining heterogeneity in a given population. It also cannot be used to identify specific variables that should be the target of interventions for particular patients. Instead, the goal of the PITE approach is to establish whether a treatment strategy affects patients differentially and to use that understanding to support treatment decisions. To that end, an advantage of PITEs is that, once estimated, they can be used to obtain predictions of potential treatment impact for any patient for whom the covariates can be measured. Online Supporting Information for this article includes details on the covariates used, the model results that allow the PITEs and predictive intervals to be estimated, and an example of estimating a PITE and predictive interval for a theoretical person who was not part of the original Look AHEAD sample.

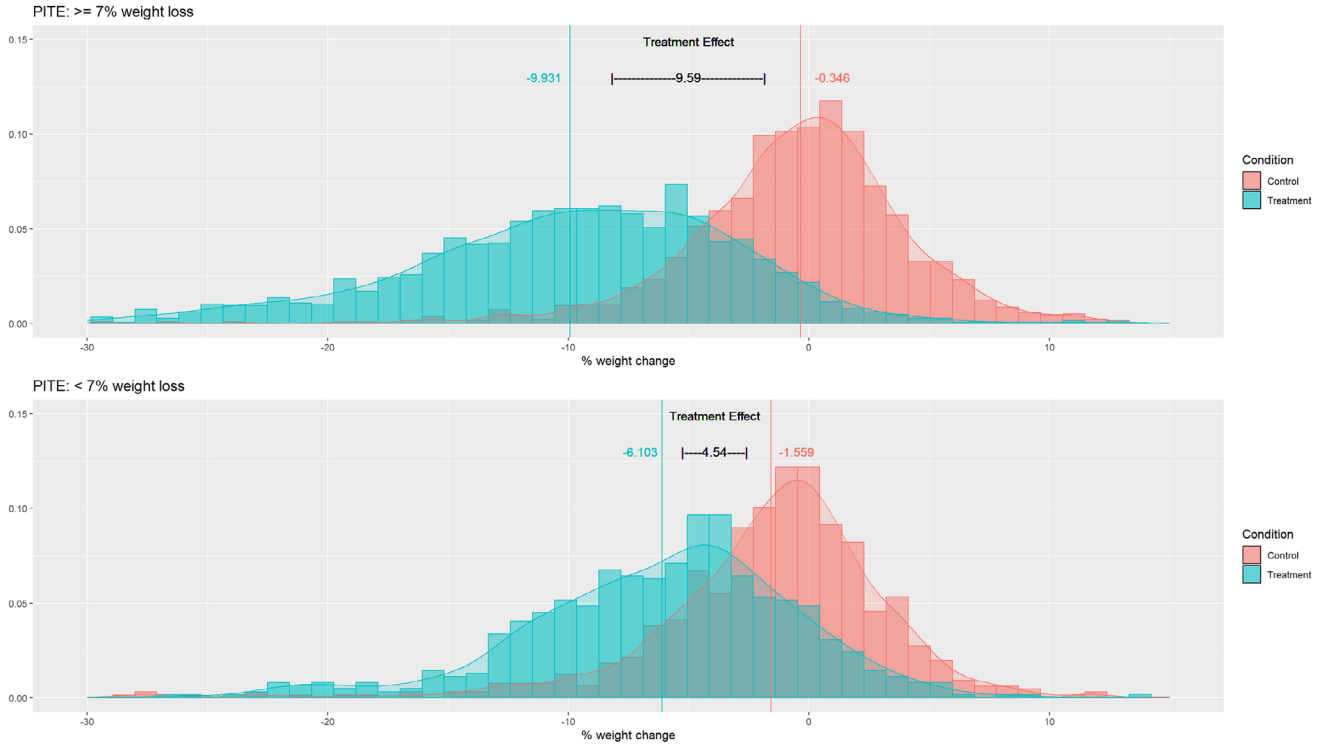

FIGURE 2 Weight loss among treatment and control conditions by subsamples predicted to lose more and less than Look AHEAD's 7% weight-loss target. Top section of figure shows the distributions of observed percentage of weight change among individuals in both treatment and control conditions who were predicted to lose 7% or more of their body weight over the course of the first year of the Look AHEAD intervention. The lower section of the figure shows the distributions of observed percentage of weight change among individual in both treatment and control conditions who were predicted to lose less than 7% of their body weight over the course of the first year of the Look AHEAD intervention. Mean percent weight change for treatment and control groups is represented by a vertical line and reported above each density curve for the appropriate group. The difference between average percent weight loss in treatment and control groups is illustrated as the treatment effect in both sections. Look AHEAD, Action for Health in Diabetes; PITE, predicted individual treatment effect.

One limitation of this work is that the generalizability of the predictive algorithm to only those patients who have been diagnosed with type 2 diabetes, as the Look AHEAD trial only recruited patients with type 2 diabetes. As such, our predictive algorithm is valid for determining the predicted benefit of the Look AHEAD intervention in patients with type 2 diabetes. Further research should examine whether predictions would be similar for those with obesity and no clinical diagnosis of type 2 diabetes.

Additionally, the Look AHEAD intervention was both uniquely intensive and tailored to the individual needs of given participants because it was oriented toward understanding the effect of weight loss on CVD events rather than simply promoting weight loss in and of itself. These distinctions set it apart from most lifestyle interventions for weight loss. As a result, generalizability of these results to other lifestyle interventions might be limited. Although we cannot assume that other lifestyle interventions will have the same levels of heterogeneity, we believe that this study's findings demonstrate that improvement in average treatment effect would be possible with personalized approaches.

An additional limitation of the approach that we describe is the simultaneous challenge of selecting variables for the development of the predictive algorithm and being limited in those choices by the data that were collected in the original trial. In particular, we included some baseline variables in our analysis that might not be commonly available in a clinical setting and did not include others that might be predictive of heterogeneity. For example, maximum metabolic equivalent of task from the graded exercise test was included as a measure of cardiorespiratory fitness, which is not commonly available in a clinical setting and does not fully assess physical activity. Although trial data did include a more holistic measure of physical activity (accelerometry), these data were only available for one-half of the sample, and the reduction of sample size would have made impossible the analyses presented here. Thus, a limitation of this study is the lack of inclusion of a metric of baseline physical activity, and future research should endeavor to include such measures.

Future validation work should consider clinical feasibility in the process of selecting baseline variables that are thought to impact heterogeneity of treatment effects. This additional consideration would help to maximize the utility of the predictive algorithm in clinical practice. Ongoing research is examining ways that predictions can be obtained without data on all of the variables included in the algorithm, which would also increase the clinical utility of the approach [36].

There is a tradeoff between the signal provided by adding more covariates during the development of the algorithm and the random

noise that is contributed by those additional variables. Including more variables in the development of the algorithm does not always lead to better predictions. The decisions of how many and which variables to include are highly dependent on the context of the outcome of interest, the intervention or treatment being tested, and data availability. Previous applications of the model have used between 19 and 53 baseline variables to develop the predictive algorithm [22, 24]. We hypothesize that a systematic approach to selection of baseline predictors that includes previous research, clinical experience and feasibility, and existing theory regarding the etiology and treatment of obesity is most likely to result in replicable results.

Furthermore, we were able to calculate PITEs for only one possible treatment that would need to be part of the decision-making process between clinicians and patients. Ideally, clinicians would be able to compare PITEs for multiple treatment options for a given patient before choosing a particular treatment route. Future applications of the method should test other obesity treatment options to enable clinicians and patients to make the most informed decisions possible when choosing among potential treatment options.

A final limitation of this analysis is that it was not possible to externally validate our predictions with an independent dataset. We did perform internal validation and present 10-fold cross-validated estimates in our results but acknowledge that the best evidence of validated predictions would require external validation. Future research with an independent sample, ideally in the context of a prospective clinical trial, should seek to externally validate these results.

CONCLUSION

Although these results only begin the process of using personalized predictions to support clinical decision-making, they come at an important time in the field in which pharmacological interventions such as those with GLP-1 receptor agonists have shown very large treatment effects. Although these interventions work well, shared decision-making between patients and health care providers requires consideration of effective treatment alternatives. The PITE approach demonstrates that weight-loss goals for some individuals can be achieved through intensive lifestyle intervention and may have future utility in the shared decision-making process after alterations to increase clinical feasibility and external validation of predictions.O

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CONFLICT OF INTEREST STATEMENT

The authors declared no conflicts of interest.

DATA AVAILABILITY STATEMENT

Data from the Look AHEAD: Action for Health in Diabetes (Look AHEAD) (Version 9, https://doi.org/10.58020/wr3g-1218) reported here are available for request at the NIDDK Central Repository (NIDDK-CR) website, Resources for Research (R4R), https://repository.niddk.nih.gov/

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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