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Human-in-the-Loop AI Digital Twin to Extend Virtual Precision Diabetes Care Between Visits: Results From a Randomized Clinical Trial

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Abbreviations

T2D: Type 2 Diabetes; **AI:** Artificial Intelligence; **ANN:** Artificial Neural Network; **OHLC:** Online Human-in-the-Loop Predictive Control; **PDT:** Predictive Digital Twin; **RNN:** Recurrent Neural Network; **LSTM:** Long-Short Term Memory; **PSO:** Particle Swarm Optimization; **RCT:** Randomized Controlled Trial; **KNN:** K-Nearest Neighbor; **TF:** Transfer Learning; **KD:** Keto Diet; **LF:** Low Fat Diet

Ethics and Dissemination

This study was conducted in accordance with the ethical principles of the Declaration of Helsinki and in compliance with U.S. federal regulations for the protection of human subjects (45 CFR 46). The study protocol was reviewed and approved by the Institutional Review Board of the University of Texas Health Science Center at San Antonio (Protocol Number: HSC20190528H).

Written informed consent was obtained from all participants (in related files). The study was registered at <http://ClinicalTrials.gov> (NCT05071287). The initial release date was 2021-06-03.

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Author Contribution

JW, YD, and KS designed the parent trial. JW, AA, SHAF, and SL designed the study. SHAF and SL conducted numerical studies. SL, JW, SHAF, YD, SL, AA, JW, YY and KS reviewed the results. JW, SHAF, YD, AA, SL, KS, and YY contributed to writing the manuscript. All authors reviewed the manuscript. KS secured funding for the study.

Data Availability

The data collected for this study, including individual participant data, will be made available upon request. The data will be shared in a deidentified format to ensure participant privacy and confidentiality. Access to the data will be granted following the approval of a detailed proposal and the signing of a data access agreement. This agreement will outline the terms of use, ensuring that the data are utilized for legitimate research purposes and in a manner that preserves the confidentiality and integrity of the data. Requests for data should be directed to Yan Du. The study protocol, statistical analysis plan, and informed consent form are accessible in the published protocol paper associated with this study.

Use of Artificial Intelligence Tools

Artificial Intelligence-based tools, including large language models, were used solely for language editing and clarity improvement of the manuscript. These tools were not involved in study design, data analysis, model development, or interpretation of results. All scientific content, analyses, and conclusions were developed and verified by the authors.

Code Availability

The code underlying the predictive digital twin and online human-in-the-loop control algorithm is not publicly available due to institutional and data security restrictions but may be made available to qualified researchers request to the corresponding author.

Conflicts of Interest

All authors declare no financial or non-financial competing interests.

Abstract

Background

Type 2 diabetes (T2D) requires sustained lifestyle support, yet health systems face workforce and visit-capacity constraints that limit ongoing coaching between encounters. We evaluated a digitally enabled “human-in-the-loop” care support model that uses a predictive AI digital twin to generate daily, personalized short message service (SMS) feedback aimed at improving lifestyle adherence while maintaining glycemic stability.

Methods

The parent trial enrolled 40 adults (≥ 18 years) with T2D in a 6-month randomized trial. Participants completed 3 months of baseline observation followed by a 3-month intervention period (6,467 longitudinal data points; mean follow-up: 174 days). For the ancillary AI intervention, a subset of participants was randomized to either receiving AI-generated daily individualized feedback or no daily feedback. The online human-in-the-loop predictive control (OHLC) model used a transfer-learning artificial neural network digital twin trained on self-monitoring data (weight, food logs, physical activity, glucose). A particle swarm optimization controller identified actionable behavior changes aligned with glucose and weight goals; the digital twin was retrained weekly to incorporate newly accrued data.

Results

The OHLC model achieved $\geq 80\%$ prediction accuracy across all diet-condition subgroups. During the 3-month AI intervention period, participants receiving AI-generated feedback exhibited a trend of improved daily steps and stable or improved total caloric and total carb intake aligned with dietary targets. Mixed ANOVA results showed that the AI intervention group exhibited significant weight loss compared with the control group (average loss: 5.871 lbs.; $p < .0001$), while maintaining stable glucose levels throughout the study period ($p = 0.661$). In contrast, the non-AI group exhibited more modest weight reduction (average loss: 3.574 lbs.).

Conclusions

This study suggests that a human-in-the-loop AI digital twin model can support weight management without compromising glycemic stability, offering a potentially scalable approach for extending precision diabetes self-management support beyond clinic visits. Larger, multi-site studies should assess implementation outcomes, access, and system-level effects on utilization, cost, and quality metrics.

Introduction

Type 2 diabetes (T2D) is a leading chronic condition worldwide and a major driver of preventable complications, healthcare utilization, and costs.¹ Effective management requires sustained lifestyle support and frequent self-management decisions across diet, physical activity, and medication adherence.² However, many health systems face challenges in delivering continuous, individualized coaching between clinic visits because of workforce shortages, limited visit capacity, and unequal access to diabetes education - factors that may exacerbate outcome disparities.^{3,4}

The digital health interventions can extend self-management support beyond the clinic, but many solutions deliver generic recommendations that are insufficiently tailored to individual patterns and preferences.⁵ Precision approaches that learn from a person's longitudinal self-monitoring data may improve relevance and engagement while reducing clinician burden. "Digital twin" models, computational representations that predict near-term physiologic outcomes based on behavior inputs, offer a pathway to individualized lifestyle guidance.⁶⁻⁸ Transfer learning can further enable such models to be trained in data-sparse settings by leveraging shared patterns across patients and then fine-tuning to subgroup- or individual-level characteristics.⁹

Most algorithmic approaches in diabetes management have focused on predicting glucose trajectories or automating insulin delivery,¹⁰⁻¹² with fewer studies evaluating AI systems designed to support lifestyle behavior change in real-world care delivery contexts.^{13,14} For health systems, the key question is not only whether an algorithm predicts outcomes accurately, but whether it can be operationalized as a low-burden intervention that improves clinically meaningful outcomes, maintains safety (e.g., glycemic stability), and scales across populations.¹⁵

In this study, we evaluated a human-in-the-loop AI intervention that uses a transfer-learned predictive digital twin and an online optimization controller to generate daily, personalized text-messaging feedback to adults with T2D. We conducted a randomized trial to assess early effectiveness on lifestyle behavior trends and weight outcomes while monitoring glycemic stability, and we describe the intervention as a health system-relevant approach for extending precision diabetes self-management support between visits.

Materials and Methods

Study design and setting

This study was a randomized trial embedded within a single-center parent randomized controlled trial (RCT).¹⁶ The parent trial enrolled overweight/obese adults and followed participants longitudinally using mobile health devices and daily self-monitoring. The present trial evaluated an ancillary AI-enabled intervention delivered during the second half of the study period.¹⁶

Participants and data collection

The parent trial enrolled 60 overweight or obese adults (≥ 18 years), including 40 participants diagnosed with T2D. Participants were assigned to a ketogenic or low-fat, low-calorie diet and self-monitored dietary intake using a smartphone-based application. Physical activity was tracked using a *Fitbit Inspire 2*, and body weight was measured using a *Withings* body scale. All participants received health education consistent with evidence-based behavioral lifestyle interventions. Participants completed a 3-month baseline observation period followed by a 3-month intervention (mean follow-up: 174 days), generating 6,467 longitudinal daily data points from self-monitoring of dietary intake, body weight, physical activity (steps), and glucose-related measures.¹⁷ These data were used to support transfer learning-based pretraining of a predictive digital twin model.

For the ancillary AI intervention, a subset of 19 adults with T2D was selected and randomized to receive either daily AI-generated individualized feedback (AI group, $n=10$) or no daily feedback (control group, $n=9$) during the 3-month intervention period. Data from the initial 3 months were used to train the predictive digital twin, after which continuously streamed data informed an online control model that generated daily recommendations delivered via short message service (SMS). The predictive model was retrained weekly to improve performance.

Model Construction: Predictive digital twin (transfer-learned ANN)

The online control model at its core utilizes an artificial neural network (ANN) predictive digital twin model that has been trained using transfer learning (TF) strategies to improve its performance (for both data rich and data scarce setup) to generate food intake suggestions.^{18,19} As a proof of concept, we have the following contributions in this work:

- A human-in-the-loop artificial intelligence feedback system.
- A transfer-learned predictive digital twin model of patients.
- An evolutionary optimization-based online control model in mHealth devices.

Figure 1 shows the overall schema of the proposed model. We first build a predictive model where inputs are the daily lifestyle choices, and the outputs are the next day's glucose and weight levels. Next, we used the predictive model as the core block for the online control model. The control model is built based on the Particle Swarm Optimization (PSO) method, which generates feedback that minimizes glucose and weight outputs. We re-trained the models every week. PSO utilizes the fine-tuned model as a core plant to generate dietary suggestions.

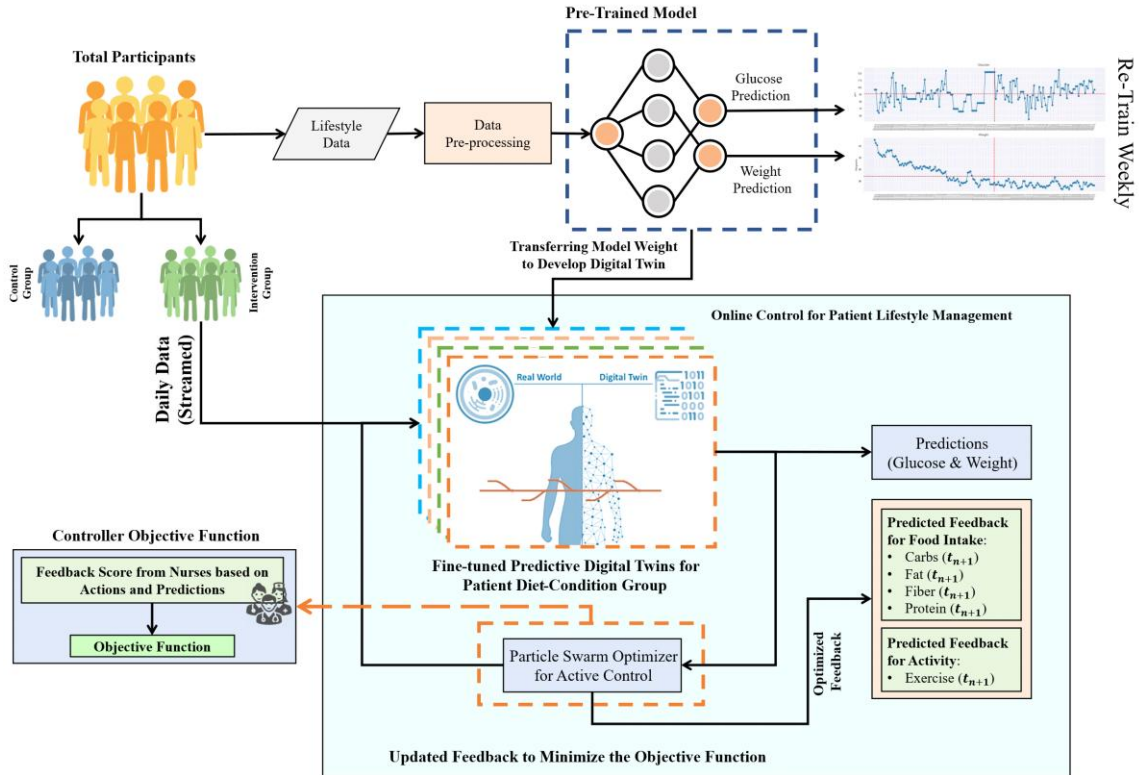


Figure 1: Overall Scheme of the proposed method.

Predictive Digital Twin: Transfer Learning-Based Artificial Neural Network to Predict Patient States

The intervention was designed as a “between-visit” self-management support model. During the 3-month baseline phase, no participants received AI feedback. At the start of the 3-month AI-intervention phase, the AI group began receiving daily personalized SMS containing actionable lifestyle suggestions (e.g., dietary and activity adjustments) generated by an online human-in-the-loop predictive control (OHLC) model. The control group continued usual self-monitoring and diet guidance without daily AI SMS.

We start by developing a predictive digital twin (PDT) that will emulate the patient's behavior. By definition, a predictive twin models the future behavior and state of any system in consideration. These models utilize historical data to incorporate possible system modes within the model. We construct the PDT to receive self-monitoring data from patients (food intake, weight, exercise regimen, etc.). This allows the twin to simulate the physical object in real-time, in the process offering insights into their performance (weight and blood glucose control).

We construct a simple multilayer perceptron/artificial neural network (with three hidden layers) (ANN) for predictive modeling of daily glucose levels using the health time series data. We utilize a transfer learning strategy to take care of the missing values. In literature, transfer learning strategies have proved to make learning from data efficient, fast, and under sparse data fruitful.¹⁹ To achieve this goal, we concatenated and sampled all the patient's data and created the transfer learning dataset to pre-train the ANN model.²⁰ Once the pre-training is done, the model is fine-tuned for each patient diet-condition group (1. *Keto Diet – Obese and T2D*, 2. *Keto Diet – Obese, Kidney Disease, and T2D*, 3. *Low-Fat Diet – Obese and T2D*, 4. *Low-Fat Diet – Obese, Kidney Disease, and T2D*). The training procedure involves sampling data to train a deep learning model for each patient group of interest, where the ANN model weights of the pre-trained model used as the prior. We compare the performance of the model with classic machine learning models (*KNN*, *Gaussian Process*, *Decision Tree*, *Random Forest*, *Gradient Boosting*). Parameters for all the models are tuned using a grid search approach. While many of the above-mentioned algorithms can be used for building the predictive twin (comparable accuracy; later shown in the results section), we selected the transfer learning (TF)-based ANN algorithm for our analysis for two specific reasons:

- They adapt to learning complex patterns present in the data, and
- The predictive twin can be trained even if there is a low amount of data (data sparsity) for a new patient group.

Figure 2 shows a visual representation of the transfer learning strategy used in this work. We followed the same steps as Faruqi et al.²⁰ The only change was that they fine-tuned their models for each patient, and we fine-tuned for each patient's diet-condition group.

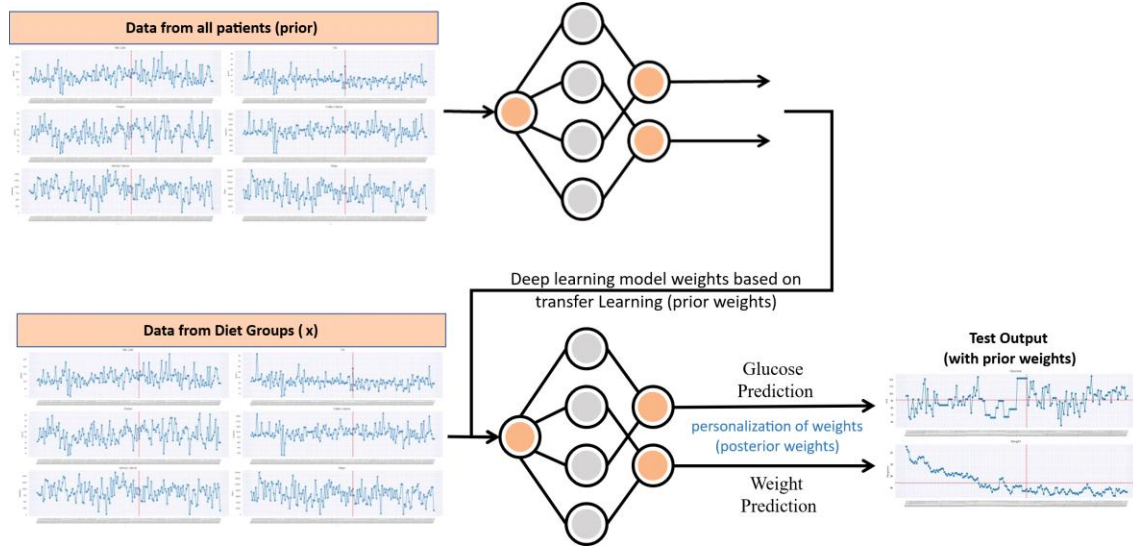


Figure 2: Scheme of the transfer learning strategy to train an artificial neural network for predictive modeling.

Online Control Model: Particle Swarm Algorithm

Once the PDT is developed, we focus on developing the control model of the proposed algorithm. The control model uses PDT (of the patient-diet group) to determine what combination of food intake and exercise would help a patient maintain their blood glucose level and help them lose weight while maintaining their blood glucose level. This highly non-linear problem needs to be optimized efficiently within the search space. We deploy the Particle Swarm Optimization (PSO)²¹ algorithm as the controller due to its simple implementation; it doesn't need a gradient form of the objective function and, depending on the setting, is less memory consuming (can be used in both online and off-line setup). For a function defined in multidimensional vector space (as in our study case), PSO is a robust meta-heuristic optimization algorithm and one of the best optimization algorithms to find the minimum or maximum of the objective function. The PSO algorithm (Step 2 of Figure 1) is then used with the predictive twin to determine the best parameters to minimize the objective function. The PSO algorithm consists of two components: (1) the Objective function and (2) The constraints.

The OHLC controller used particle swarm optimization (PSO) to identify feasible behavior changes that minimize predicted risk while supporting weight goals and glycemic stability. Constraints for macronutrient recommendations were defined based on diet requirements and clinical team input, enabling clinically sensible search boundaries. Human-in-the-loop input was incorporated as a penalty factor that increased the cost of implausible or undesirable recommendations, allowing nursing expertise to improve safety and appropriateness. The PDT was retrained weekly during the intervention period to incorporate newly accumulated data and adapt guidance over time.

The Objective Function

To set up PSO for our study, we need an objective function that helps us achieve our goal. For a patient in the low-fat diet group, our goal is to suggest a food and exercise regimen that can help them lose weight (W) till they reach their target weight level ($W_G = W_0 - 0.2W_0$). Once they reach their target level, we switch the goal to maintaining that weight. The patients will also need to maintain their Glucose levels (G) within an acceptable range ($70 \leq G \leq 130$). A patient in the keto diet group must attain (or close to) a certain blood ketosis level. To do that, they need to reach a keto ratio (K) of 1.5 or higher. The keto ratio can be computed from the suggested food intake (macronutrients) by the PSO algorithm. The objective function is special in the sense that we don't want the algorithm to select extreme parameters (in our case,

food intake and physical activity suggestions) that cause the glucose level to go near zero or too much of a higher ketone level. To resolve this issue, we introduced a tuning parameter λ , which takes the value of 0 whenever a generated suggestion reaches its desired value; otherwise, it takes a value of 1. This helped control the model to achieve its desired output. We integrated the feedback of the nursing knowledge using a second multiplier (penalty factor, m) for each element of the objective function. Depending on the suggestion provided by the controller, if the predicted glucose/weight/ketone level is too diverse, a nurse can assign a higher penalty and vice versa. In our case, this assigned score ranged from 1 to 1000 to penalize the model if it's too far away from desired values. At the end of each evaluation phase, the score derived from nursing knowledge is assigned to the model. The details of the decision boundaries considered by the nurses are provided in **Appendix 1**. Thus, considering the above, the objective function for the PSO algorithm is set as below:

Objective Function

$$\min_{l=1, \dots, L} \sum_{i=1}^n \lambda_1 m_1 \hat{G}_i + \lambda_2 m_2 \hat{W}_i + \lambda_3 m_3 (1.5 - K_i)$$

Where,

Tuning parameter,

$$\lambda_1 = 0; \text{ if } 70 \leq \hat{G}_i \leq 130$$

$$\lambda_2 = 0; \text{ if } (W_i - \hat{W}_i) \geq 0 \text{ or } W_G = \hat{W}_i$$

$$\lambda_3 = 0; \text{ if } \text{Patient-Diet Group} = \text{'keto-diet'} \text{ or } (1.5 - K_i) \geq 0$$

$m_{i=\{1,2,3\}}$ = Score assigned by a human-in-the-loop. This is used in conjuncture with the tuning parameters ($\lambda_{i=\{1,2,3\}}$)

$$K = \frac{f_a}{(c - f_b + p)}; K = \text{Keto ratio}, c = \text{carb}, f_a = \text{fat}, f_b = \text{fiber}, p = \text{protein}$$

$$W_G = W_0 - 0.2W_0; W_G = \text{Weight Goal}, W_0 = \text{Patients weight at the start of the study}$$

The scores (m) assigned by the human in the loop can also be automated future studies by:

1. Building a lookup table generated by the nurse/s for all the factors to be used during the optimization session.
2. Building an approximation linear function by using the lookup table. That way, we can approximate the penalty factors even if there is a value present that wasn't assigned a penalty by the nurse/s.

The Constraints

Furthermore, we also define the search space for the proposed model. The model constraints are decided based on the appropriate diet requirement^{22,23} and discussions with human (nurse-led research team) in the loop. The constraints may also be adapted (*exception case*) based on patient specific needs based on their physical condition and nutritional needs, thus making the model adaptive not only patient group specific but also patient specific. For this work, the general constraints were defined as follows in **Table 1**:

Table 1: General Constraints for Low-Fat and Ketogenic Diet Groups

Low-Fat Group	Keto Group

$195 \leq c \leq 300$	$20 \leq c \leq 50$
$20 \leq f_a \leq 55$	$90 \leq f_a \leq 200$
$20 \leq f_i \leq 50$	$20 \leq f_i \leq 50$
$100 \leq p \leq 160$	$30 \leq p \leq 110$

Outcomes

The primary study outcomes were (1) weight change during the intervention period and (2) glycemic stability over time. Model performance was evaluated using Clark Error Grid analysis, reported as the percentage of predictions falling in Zone A.

Statistical analysis

We used mixed ANOVA to evaluate intervention effects on weight change over time and to assess glucose stability across the study period. Model performance comparisons were summarized using Clark Error Grid Zone A accuracy across diet-condition subgroups.

Results

Demographics

The sample included 19 participants, of whom 52.6% identified as male and 47.4% as female. Most participants identified as Hispanic White (47.4%). Educational attainment varied, with 42.1% reporting some college, 26.3% holding a graduate degree or higher, and 31.6% having a high school diploma or college degree. Nearly half of participants reported a household income of \$60,000 or more (47.4%). The majority were married (68.4%), while 21.1% were divorced and 10.5% never married (See Table 2).

Table 2: Demographic and Socioeconomic Characteristics of Participants

Socio-demographics	Total (N = 19)
Age, Mean (SD)	58 (10)
Gender Identity, N (%)	
Male	10 (52.6%)
Female	9 (47.4%)
Race, N (%)	
Hispanic White	9 (47.4%)
Non-Hispanic White	6 (31.6%)
Hispanic Native American	2 (10.5%)
Non-Hispanic Native American	0 (0)
Hispanic other	2 (10.5%)
Education Level, N (%)	
High school graduate	3 (15.8%)
Some college	8 (42.1%)
College graduate	3 (15.8%)
Graduate degree or higher	5 (26.3%)

Household Income, N (%)	
Under \$20,000	3 (15.8%)
\$20,000 - \$39,999	3 (15.8%)
\$40,000 - \$59,999	4 (21.1%)
\$60,000 or more	9 (47.4%)
Marital Status, N (%)	
Never married	2 (10.5%)
Married	13 (68.4%)
Divorced	4 (21.1%)

Evaluation of predictive digital twin performance

We considered two variations of the proposed predictive twin model. The two variations are (1) The base ANN (without transfer learning) and (2) ANN-TF (with transfer learning). Several baseline methods are used to compare the performance of the proposed model. All the models are tuned using a grid search approach.

To evaluate the performance of the proposed model, we trained it using the first three months of data, during which no intervention was performed in both groups. We used one month of test data immediately following the third month's intervention. Although not explicitly included in the reported evaluation (as shown in Table 3), the PDT utilized for the control model was re-trained at the end of each week as the patient's new data became available. We evaluated all the models using Clark Error Grid.²⁴ **Table 3** summarizes the percentage of prediction that falls on Zone A of the Clark Error Grid for all comparing methods.

Table 3: Prediction accuracy of the proposed neural network models along with other comparing methods based on Clark Error Grids zone A.

Model	Keto Diet Group		Low-Fat Diet Group	
	Obese + Diabetes	Obese + Kidney + Diabetes	Obese + Diabetes	Obese + Kidney + Diabetes
	Glucose Level	Glucose Level	Glucose Level	Glucose Level
KNN Regression (Weight: Distance)	77.50%	77.50%	77.50%	77.50%
KNN Regression (Weight: Uniform)	77.78%	77.78%	77.78%	77.78%
Gaussian Process (Kernel: RBF)	76.94%	76.94%	76.94%	76.94%
Decision Tree	71.67%	71.67%	71.67%	71.67%
Random Forest	84.17%	84.17%	84.17%	84.17%
Gradient Boosting	84.44%	84.44%	84.44%	84.44%
Artificial Neural Network (ANN)	79.72%	87.44%	87.78%	84.23%
ANN (with Transfer Learning)	80.00%	87.85%	87.22%	84.90%

The proposed model, ANN-TF, performs the best, followed by ANN, Gradient Boosting, and Random Forest. Both Random Forest and Gradient Descent showed significant performance (84.17% and 84.44%) in predicting the blood glucose level for patients in the Keto-Diet group with obesity and Diabetes. They are competitive with the proposed ANN-TF model for patients with a Low-Fat Diet group with obesity.

Kidney disease and Diabetes (84.17% and 84.44%). Compared to these, the all-other method falls below 80% in performance, especially the Decision Tree, which has the lowest prediction performance (71.67%) across all the patient groups. Therefore, based on the evaluation in Table 1 (also considering the advantage of transfer learning whenever the data is sparse) and ease of use for control steps, we decided to utilize the ANN-TF model as the core/plant digital twin for the control model.

Evaluation of the Control Model

To evaluate the performance of the control model and its effect on patients, we separated the study patients into two sub-groups (as mentioned earlier).

- Group 1 started receiving feedback from the proposed model daily (intervention group), and
- Group 2 did not receive any feedback from the model (control model). The participants didn't receive any feedback for the first three months of the study.

After the first in-person intervention (at month three), group 1 started receiving daily feedback SMS. Group 2 continued to follow their suggested diet (the same diet they followed the first three months).

This was an online setup, so we continued to receive patients self-monitoring data daily, and based on that, we continued to provide them with daily food and exercise feedback for three months. **Figure 3** shows the evaluation results of self-monitored lifestyle data for the patients in this study between two groups. It shows the average monthly breakdown of the collected self-monitored data, including patients' average daily steps, daily caloric intake, total carb, and fat consumed across two distinct groups among the patients adhering to either a ketogenic diet or a low-fat diet.

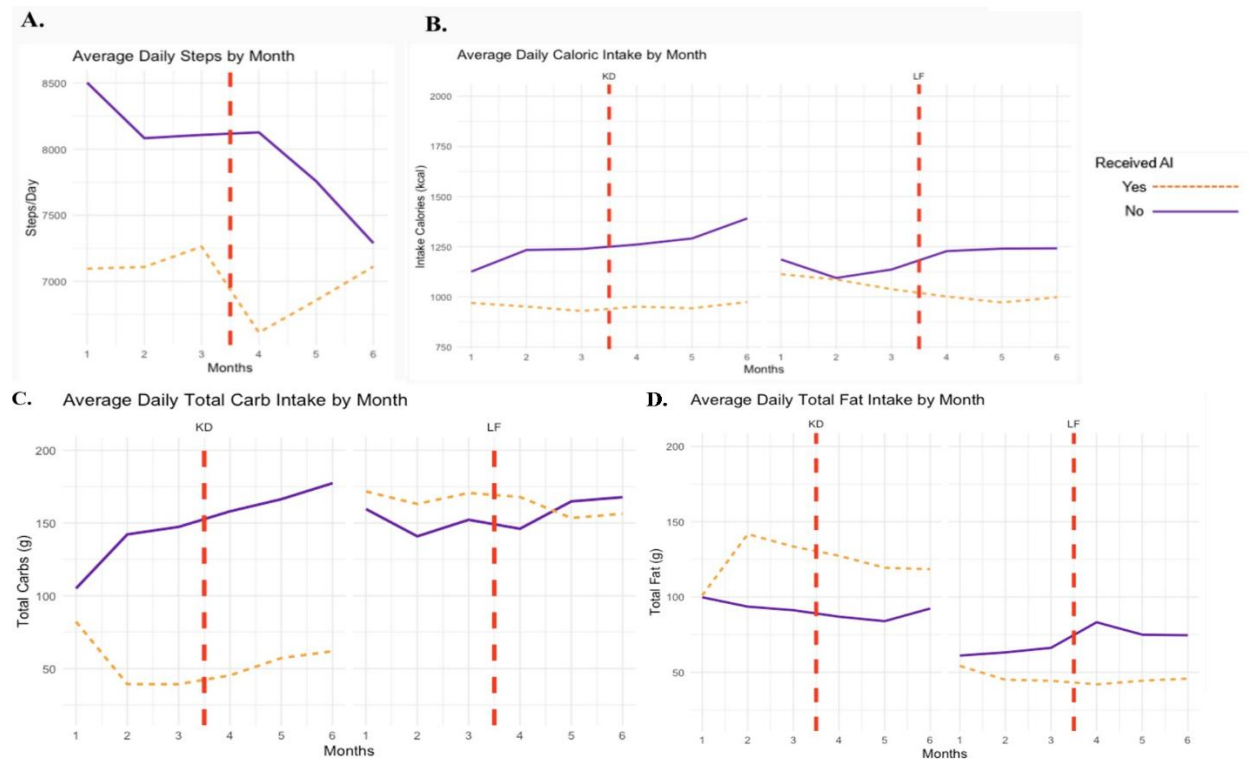


Figure 3: Self-monitored lifestyles data of a. average daily steps by month; b. daily caloric intake by month between keto (KD) and low-fat (LF) group; c. daily total carb intake by month between KD and LF group; and d. daily total fat intake by month between KD and LF group. Red dash vertical lines meant the time point (3-month) AI SMS started to be sent out.

Clinical outcomes: weight change and glycemic stability

The non-AI (control) group demonstrated a modest but statistically significant reduction in body weight (mean decrease = 3.57 lbs., $p = 0.013$), while the AI intervention group experienced a larger and statistically significant weight reduction (mean decrease = 5.87 lbs., $p = 0.012$). Although weight loss occurred in both groups, the magnitude of reduction was greater in the AI intervention group. In contrast, glucose levels remained stable over time in both the AI and non-AI groups, with no statistically significant changes observed from baseline ($p > 0.05$). With respect to goal attainment, four participants in the AI group achieved their assigned weight goals, including the highest observed weight loss of 14.82%, compared with two participants in the non-AI group, whose maximum weight loss was 8.36%. Overall, these findings suggest that AI-generated feedback may enhance engagement and support greater adherence to lifestyle modifications, particularly with respect to weight management, while maintaining stable glucose levels (See **Figure 4**).

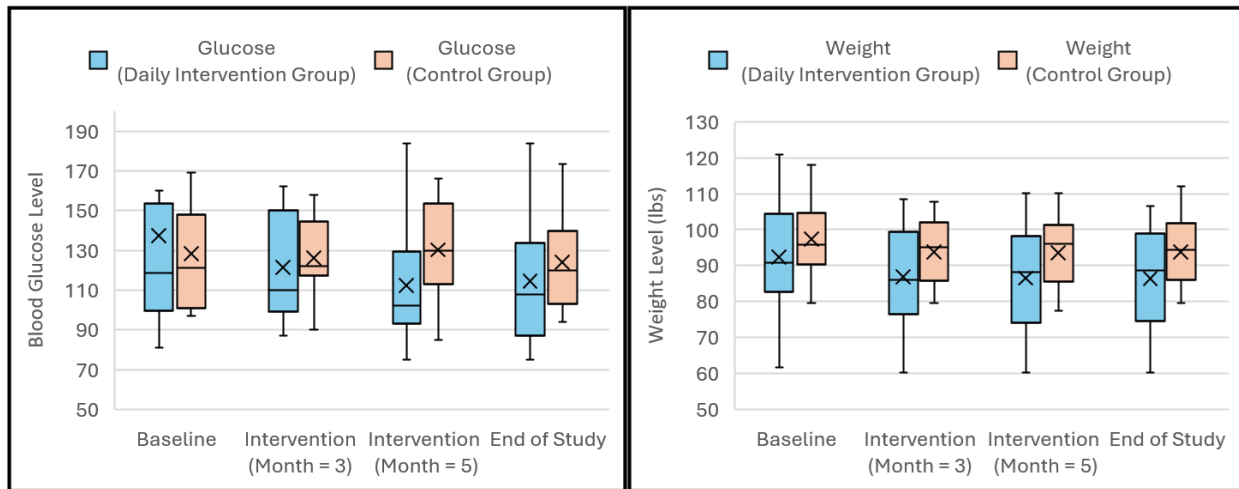


Figure 4: Weight and Glycemic Change of AI and non-AI Groups

Discussion

The objective of this study was to evaluate the effectiveness of an OHLC integrated with a predictive digital twin (PDT) in delivering continuous, individualized feedback to adults with T2D to support adherence to healthy lifestyle behaviors between clinic visits. To achieve this aim, we developed a transfer learning-enabled artificial neural network (ANN-TF) that serves as the core of the PDT. Leveraging patients' self-monitored data, the PDT learns individualized patterns of glucose and weight dynamics, enabling the development of adaptive control models that more accurately estimate behavioral and physiological targets relevant to weight and glycemic management.

By integrating the PDT with a particle swarm optimization-based control algorithm, the OHLC generates dynamic, personalized recommendations tailored to each patient's lifestyle, dietary patterns, and physical activity levels. This personalization is critical for identifying effective interventions in T2D management, where inter-individual variability substantially influences outcomes.²⁵ Nurse-assigned scores were incorporated into the loss function as a human-in-the-loop safeguard to align AI-generated recommendations with clinical judgment and support steady, sustainable behavior change. Among evaluated modeling approaches, ANN-TF demonstrated the strongest predictive performance, followed by the base ANN, gradient boosting, and random forest models, all of which may serve as viable PDT architectures depending on computational constraints.

Analysis of self-monitored data revealed distinct differences between AI and non-AI groups in physical activity, dietary intake, and weight outcomes. Participants receiving AI-generated feedback achieved significantly greater weight loss than controls, indicating the effectiveness of the OHLC framework in promoting behaviors conducive to weight management. Importantly, glucose levels remained stable across both groups, suggesting that improvements in weight and lifestyle adherence were achieved without compromising glycemic control.

This randomized trial evaluated a human-in-the-loop, AI-enabled digital twin intervention delivered via daily SMS, designed to extend precision diabetes self-management support between clinic encounters. In the context of health systems facing workforce shortages and limited visit capacity, the intervention represents a scalable care-delivery approach that may augment traditional diabetes management without requiring continuous synchronous clinician involvement. The robust performance of the transfer-learned PDT across diet-condition subgroups further supports its applicability in settings with limited individual-level data.

From a health systems perspective, several features enhance potential implementation. SMS-based delivery minimizes access barriers and integrates readily into existing chronic disease management workflows; weekly model retraining enables ongoing personalization as patient data evolve; and human-in-the-loop penalties provide a safety layer that complements clinical oversight. The system is intended as a supportive coaching extension rather than a replacement for clinician decision-making.

Future research should evaluate implementation and equity outcomes critical to health system impact, including patient engagement and adherence to self-monitoring, differential effectiveness across subgroups, workflow burden associated with oversight and escalation, and downstream utilization outcomes such as acute care visits, medication changes, and total cost of care. Multi-site studies with longer follow-up are needed to assess sustainability, scalability, and effects on quality metrics relevant to payers and healthcare delivery systems.

Limitations

This study has limitations. First, the ancillary trial included a small sample ($n=19$) from a single center, limiting generalizability and increasing risk of imbalance between groups. Second, the follow-up period was relatively short, and long-term sustainability of behavior change is unknown. Fourth, glucose and weight are influenced by factors beyond lifestyle (e.g., medications, comorbidities, social determinants), which were not fully modeled. Accordingly, findings should be interpreted as early evidence supporting feasibility and potential effectiveness, with the primary contribution being proof-of-concept for a scalable between-visit support model rather than definitive clinical effectiveness.

Conclusions

A human-in-the-loop AI digital twin intervention delivered via daily SMS improved weight outcomes while maintaining glycemic stability in adults with T2D, suggesting a scalable approach to extend precision diabetes self-management support between clinic visits. By combining transfer learning, online optimization, and nursing-informed safeguards, the model offers a potentially deployable digital health strategy for health systems seeking low-burden interventions to strengthen chronic disease management. Larger multi-site evaluations should assess implementation outcomes, equity, utilization, cost, and quality metrics to determine real-world health system value.

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