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Machine Learning Prediction of Postprandial Glucose Excursion, Exposure, and Recovery in Prediabetes: An Exploratory Secondary Analysis

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Abstract

Postprandial glucose responses in prediabetes vary in magnitude, cumulative exposure, and recovery, yet prediction studies have largely focused on excursion magnitude. We evaluated these complementary dimensions in an exploratory secondary analysis of 109 meal events from 12 adults with prediabetes and overweight or obesity who participated in a previously conducted study of individualized nutrition therapy. Food-record nutrient data were linked to continuous glucose monitoring (CGM), and outcome-specific machine learning models used baseline clinical characteristics, pre-meal CGM information, and meal macronutrient composition. Four outcomes were evaluated: acute glucose excursion, positive incremental area under the glucose curve (iAUC), delayed recovery beyond two hours, and continuous glucose recovery time to baseline within four hours (GRTB-4h). Chronological within-participant holdout evaluation yielded R^2 values of 0.78 for acute excursion, 0.65 for positive iAUC, and 0.27 for continuous GRTB-4h; delayed-recovery classification achieved a receiver operating characteristic area under the curve (ROC-AUC) of 0.83. Recovery occurred within two hours after 35.78% of meals and between two and four hours after 41.28%, whereas 22.94% had no observed qualifying recovery by four hours.

These preliminary findings support evaluating recovery alongside excursion and exposure in postprandial glucose prediction, while larger independent cohorts are needed to establish generalizability.

Keywords: prediabetes; postprandial glycemic response; continuous glucose monitoring; machine learning; glycemic recovery; personalized nutrition

1 Introduction

Diabetes affected an estimated 589 million adults aged 20-79 years worldwide in 2024, and this number is projected to reach approximately 853 million by 2050 [1]. Prediabetes is a high-risk intermediate state of glucose dysregulation and an important opportunity for early lifestyle intervention. Although fasting glucose and glycated hemoglobin (HbA1c) remain central to screening and monitoring, these measures do not fully characterize the dynamic glycemic response to meals. The postprandial glucose response therefore provides complementary information that may help identify metabolic heterogeneity and inform individualized dietary management.

Postprandial dysglycemia is clinically relevant because elevated glucose after meals has been associated with cardiovascular risk, oxidative stress, and endothelial dysfunction [2, 3]. Individuals with similar HbA1c values may nevertheless exhibit substantially different glucose excursions and recovery patterns after eating. Continuous glucose monitoring (CGM) makes these differences observable under free-living conditions. For example, CGM has revealed marked glucose variability and excursions into prediabetic or diabetic ranges even among individuals classified as normoglycemic using conventional measures [4]. More recently, the shape of CGM glucose curves during standardized at-home oral glucose tolerance tests (OGTTs) was shown to contain information about distinct metabolic subphenotypes, including patterns related to insulin resistance and beta-cell or incretin dysfunction [5]. These findings indicate that the postprandial glucose trajectory contains information that is not captured by a single fasting or long-term average measure.

Substantial inter-individual variability also occurs in response to the same foods. Zeevi and colleagues monitored 800 individuals across 46,898 meals and observed markedly different postprandial glucose responses to identical meals [6]. A machine learning model combining dietary, clinical, anthropometric, and gut microbiome features improved prediction relative to carbohydrate-based approaches, and model-guided dietary recommendations reduced postprandial responses in a subsequent intervention [6]. Similarly, the PREDICT 1 study of 1,002 twins and unrelated adults reported a population coefficient of variation of 68% for glucose responses to identical meals and showed that both meal composition and person-level characteristics contribute to postprandial glycemia [7]. In a randomized trial involving 225 adults with prediabetes, a diet designed to target individually predicted postprandial responses improved glycemic control more than a Mediterranean diet, with benefits maintained during follow-up [8]. Collectively, these studies support the value of individualized prediction for precision nutrition.

Most prediction studies, however, have represented the postprandial response using a single outcome, commonly the glucose peak or an area-under-the-curve measure. Recent studies illustrate this emphasis. A transformer-based model applied to 58 adults receiving multiple daily insulin injections predicted postprandial glucose peaks with a mean absolute error of 32.2 mg/dL and an R^2 of 0.58, with carbohydrate-based inputs performing comparably to the full nutrient model [9]. In another study, personalized models trained on prior observations from 67 adults with type 2 diabetes predicted subsequent postprandial excursions using CGM data alone or in combination with self-reported meal and medication information [10]. Although these approaches demonstrate the feasibility of personalized prediction, they do not jointly distinguish the magnitude of the initial glucose excursion, cumulative postprandial glucose exposure, and recovery duration.

The magnitude, cumulative exposure, and recovery components of the postprandial glucose response are related but not interchangeable. Two meals may produce similar peak excursions while differing substantially in their total glucose exposure or the time required for glucose to return to a defined threshold relative to the glucose concentration at meal initiation. Conversely, a modest peak may be followed by a prolonged elevation. Acute glucose excursion characterizes the maximum increase above the glucose concentration at meal initiation, whereas positive incremental area under the glucose curve (positive iAUC) summarizes cumulative postprandial glucose exposure above this concentration until the first return to the meal-initiation glucose level or up to four hours if no return occurs. Delayed recovery beyond two hours indicates whether glucose has failed to reach the defined recovery threshold within two hours after meal ingestion. Continuous glucose recovery time to baseline within four hours of meal ingestion (GRTB-4h) provides a complementary temporal measure that is directly interpretable in minutes [11]. Evaluating these complementary outcomes may therefore provide a more complete characterization of postprandial glucose regulation and reveal whether their predictability and associated predictor patterns differ.

In this study, we used data from a randomized controlled trial of individualized nutrition therapy incorporating CGM feedback in adults with prediabetes and overweight or obesity [12, 13] to develop machine learning models for four analytical outcomes representing three dimensions of the postprandial response: acute glucose excursion (magnitude), positive incremental area under the glucose curve (positive iAUC; cumulative postprandial glucose exposure), and glucose recovery, represented by delayed recovery beyond two hours and continuous GRTB-4h. Meal events were reconstructed by aligning nutrient data from Nutrition Data System for Research (NDSR)-analyzed food records with CGM traces. Predictors were restricted to baseline clinical characteristics, pre-meal CGM measures, and meal macronutrient composition so that the models relied only on information available at or before meal ingestion. Delayed recovery was modeled as a binary representation of the recovery dimension according to whether the defined recovery threshold was reached within two hours. GRTB-4h was modeled as a continuous outcome among meals with an observed recovery within four hours; meals without an observed recovery were not assigned an artificial continuous recovery time. Our aims were to assess whether the postprandial outcomes could be predicted from dietary, clinical, and pre-meal CGM data; compare

the predictors selected for each outcome; evaluate the direction of prediction errors for the continuous outcomes; and characterize the timing of postprandial glucose recovery. Given the modest participant sample and the absence of external participant-level validation, the present work was designed as an exploratory feasibility analysis intended to evaluate whether these complementary CGM-derived outcomes could be modeled from routinely collected inputs.

2 Materials and Methods

This section describes the analytical framework used to construct the meal-level dataset and develop supervised machine learning models for the four postprandial glucose-response outcomes. The methodology encompasses clinical and dietary data preprocessing, engineering of the CGM-derived predictive targets, feature construction, and development and validation of four outcome-specific machine learning pipelines representing acute glucose excursion, cumulative postprandial glucose exposure, and glucose recovery time.

2.1 Study Population and Dataset Characteristics

The data used in this predictive modeling study were derived from a randomized controlled trial evaluating individualized nutrition therapy (INT) combined with CGM in adults with prediabetes and overweight or obesity [12, 13]. Eligible participants were 45-65 years of age, had a baseline HbA1c concentration between 5.7% and 6.4%, and had a body mass index (BMI) between 25.0 and 39.9 kg/m^2 [12]. Individuals were excluded if they had active cancer; thyroid, kidney, liver, or pancreatic disease; or were participating in a concurrent weight-loss program. Full details of the parent trial design, recruitment procedures, eligibility criteria, and intervention have been reported previously [12]. The parent trial was conducted in accordance with the Declaration of Helsinki and was approved by the George Mason University Institutional Review Board, and the present secondary analysis was reviewed and determined to be exempt [12]. Informed consent was obtained from all participants enrolled in the parent trial.

Dietary intake was assessed using food records collected prospectively over approximately 30 days. Participants used standardized, study-provided forms to record all foods and beverages consumed during the study period. For each eating occasion, participants documented the date and time; detailed descriptions of the foods and beverages consumed; portion sizes using household measures or natural units when possible; preparation methods; the main ingredients and their portion sizes for combination foods, when available; applicable brand names; and the person responsible for food preparation. The food-record data were analyzed at the eating-occasion level using the NDSR, and each eating occasion was matched to its corresponding postprandial glycemic response captured by CGM.

The dataset available for the present secondary analysis initially included 21 participants with dietary and CGM data. Recorded eating occasions were subsequently aligned with the corresponding CGM traces and subjected to the meal-level signal-quality criteria described in Section 2.2. Meal windows with insufficient CGM coverage

were excluded. After completion of the meal-CGM alignment and signal-quality preprocessing, 12 participants remained in the final meal-level analytic dataset. Additional outcome-specific eligibility criteria for the machine learning analyses, including the minimum number of eligible meals required per participant for the within-participant training and holdout procedure, are described in Section 2.5.

To minimize temporal information leakage, only clinical measurements obtained at baseline, before the intervention, were considered as baseline model inputs. These measurements included HbA1c (%), OGTT glucose concentration (mg/dL), percent body fat (PBF; %), and dry lean mass (DLM; kg).

The resulting meal-level analytic dataset comprised 109 eligible meal events from 12 participants. The baseline demographic and clinical characteristics of these participants are reported in Section 3.1.

2.2 Data Preprocessing and Target Engineering

To construct the meal-level dataset, dietary timestamps from the food records were computationally aligned with the corresponding CGM traces. For each recorded meal, a six-hour observation window was extracted, extending from two hours before to four hours after meal ingestion. Meal windows containing fewer than 55 CGM readings across the six-hour interval or fewer than five post-meal CGM readings were excluded. These thresholds were used as minimum reading-count criteria to exclude sparsely sampled meal windows.

The glucose concentration at meal initiation was defined as the CGM reading closest in absolute time to the recorded meal-ingestion timestamp. Using this meal-specific reference glucose concentration, four analytical outcomes representing three dimensions of the postprandial response were constructed: glucose-excursion magnitude, cumulative postprandial glucose exposure, and glucose recovery time.

Target 1 (T1): Acute Glucose Excursion. The acute glucose excursion was defined as the maximum glucose concentration observed during the four-hour post-meal window minus the glucose concentration at meal initiation. This outcome was expressed in mg/dL and represented the maximum observed change in glucose concentration relative to the meal-initiation value.

Target 2 (T2): Positive iAUC. The cumulative postprandial glucose response was quantified using the positive iAUC [14, 15]. Cumulative postprandial glucose exposure was expressed as mg/dL·min and calculated as the positive incremental area above the glucose concentration at meal initiation. Only glucose values above the glucose concentration at meal initiation contributed to the integral, with the calculation extending from meal ingestion until the first return to the glucose concentration at meal initiation or up to 4 hours if this concentration was not reached. The 4-hour postprandial window was selected because glucose concentrations are generally expected to return toward the initial baseline within approximately 2-3 hours under normal glucose regulation, while a longer window permits characterization of prolonged responses [11].

Targets 3 and 4: Glucose Recovery. Glucose recovery was evaluated using two related outcomes derived from the same operational recovery definition: Target 3 (T3), continuous glucose recovery time to baseline within four hours (GRTB-4h),

and Target 4 (T4), delayed glucose recovery beyond two hours. T3 quantified the observed recovery time in minutes among meals for which recovery occurred within the four-hour observation window, whereas T4 represented the same recovery process as a binary outcome according to whether recovery occurred within two hours.

Target 3 (T3): Continuous Glucose Recovery Time to Baseline within Four Hours. GRTB-4h was operationalized as an adaptation of the GRTB concept introduced by Kinny et al. [11] for application to free-living postprandial meal responses. In the present analysis, GRTB-4h was defined as the elapsed time from meal ingestion to the first CGM reading occurring after the observed post-meal glucose peak at which glucose was at or below 5 mg/dL above the glucose concentration at meal initiation. Restricting the search to readings after the observed peak prevented an early fluctuation near the meal-initiation glucose concentration, before the glucose rise, from being incorrectly classified as recovery. Recovery time was based on the first qualifying observed CGM reading; interpolation between consecutive readings was not used. This operational definition differs from the original stability-based GRTB implementation, which used consecutive CGM readings and a 2.5 mg/dL deviation criterion; here, recovery was identified using the first qualifying post-peak reading and the prespecified 5 mg/dL threshold relative to the glucose concentration at meal initiation [11].

The search for recovery was bounded by the four-hour post-meal observation window. Meals with an observed qualifying recovery were assigned their continuous GRTB-4h value. Meals without an observed recovery by four hours were not assigned an artificial continuous recovery time and were therefore excluded from the T3 analysis. For descriptive characterization, recovery was additionally classified as occurring within two hours, between two and four hours, or not observed by four hours. Among meals that recovered between two and four hours, the additional recovery time beyond the two-hour point was calculated as GRTB-4h minus 120 minutes.

Target 4 (T4): Delayed Glucose Recovery Beyond Two Hours. T4 represented glucose recovery as a binary outcome derived from the same GRTB-4h recovery definition used for T3. T4 was coded as 0 when the defined recovery threshold was reached within 120 minutes of meal ingestion and as 1 when the recovery threshold was not reached within 120 minutes. Meals that recovered between two and four hours were therefore assigned to the delayed-recovery class. Meals without an observed recovery by four hours were also assigned to the delayed-recovery class because the available CGM data established that recovery had not occurred within the first two hours, even though their exact recovery times were unknown. Thus, T4 did not require assigning an artificial continuous recovery time to meals without an observed four-hour recovery.

Together, T1 and T2 characterized the magnitude and cumulative exposure of the postprandial glucose response, respectively, whereas T3 and T4 characterized the glucose-recovery process using continuous and binary representations, respectively. The predictors considered for these outcomes were constructed as described in Section 2.3, and the corresponding regression and classification models were developed using the outcome-specific architectures described in Section 2.4.

2.3 Feature Engineering

Predictors were restricted to meal composition, glucose at meal initiation, pre-meal CGM measurements, and baseline clinical characteristics, without incorporating the subsequent postprandial glucose response. The directly measured meal-composition variables included total carbohydrates, total fat, total protein, total dietary fiber, and total energy. Several additional variables were engineered to represent the absolute and relative macronutrient composition of each meal.

Digestible carbohydrates were calculated by subtracting total dietary fiber from total carbohydrates. The protein-to-carbohydrate and fat-to-carbohydrate ratios were calculated by dividing total protein and total fat, respectively, by total carbohydrates. The carbohydrate-to-fiber ratio was calculated by dividing total carbohydrates by total dietary fiber. A constant of 10^{-5} was added to the denominator of each ratio to prevent division by zero while having a negligible effect on the calculated values for meals with nonzero carbohydrate or fiber content. The proportion of meal energy supplied by carbohydrates was calculated by multiplying total carbohydrates by 4 kcal/g and dividing the result by the total energy content of the meal, with 10^{-5} similarly added to the denominator. These variables were considered because meals with similar absolute carbohydrate contents could differ in their relative protein, fat, fiber, and energy composition.

In addition to meal composition, the glucose trajectory immediately preceding the meal was represented by the *Pre-Meal Glucose Slope*. This variable was calculated as the difference between the glucose concentration at meal initiation and the earliest available glucose concentration within the two-hour pre-meal window, divided by two hours. The resulting value was expressed in mg/dL per hour. Positive values indicated that glucose was increasing before meal ingestion, negative values indicated that glucose was decreasing, and values near zero indicated a relatively stable pre-meal glucose trajectory.

A Composite Glycemic Load (CGL) proxy was also constructed to combine multiple aspects of meal composition into a single candidate predictor. The CGL proxy was calculated as follows:

$$\mathrm{CGL} = \frac{\text{Digestible Carbohydrates}^2}{\text{Total Fat} + \text{Total Protein} + \text{Total Dietary Fiber} + 1} \tag{1}$$

This formulation allowed the CGL proxy to increase nonlinearly with the digestible carbohydrate content of the meal while accounting for the accompanying fat, protein, and dietary fiber content. The constant +1 was added to the denominator to prevent division by zero. The CGL was treated as an analysis-specific predictive feature motivated by the general concept of glycemic load [16], rather than as an established clinical measure.

The final candidate predictor set included glucose at meal initiation, digestible carbohydrates, pre-meal glucose slope, total fat, total protein, total dietary fiber, total energy, the engineered macronutrient ratios, the carbohydrate energy proportion, the CGL proxy, and the baseline clinical characteristics described in Section 2.1. No post-meal CGM measurements or post-baseline clinical measurements were included as predictors. These candidate features were subsequently evaluated separately for each

continuous and binary response using the model-development procedures described in Section 2.5.

2.4 Outcome-Specific Machine Learning Architecture

Because the four analytical outcomes represented complementary aspects of three dimensions of postprandial glucose regulation, a separate modeling pipeline was developed for each outcome. T1-T3 were modeled as continuous responses using regression algorithms, whereas T4 was modeled as a binary response using classification algorithms. The pipelines differed in their feature-scaling procedures, target transformations, inclusion of participant identifiers, and learning algorithms. Feature selection, hyperparameter optimization, and model validation were performed separately for each target, as described in Section 2.5.

Pipeline 1: Participant-Aware Acute Glucose Excursion Regression. T1, the acute glucose excursion, was modeled using a participant-aware architecture. Continuous numeric predictors were transformed to the range from zero to one using min-max scaling. The participant identifier was additionally represented through one-hot encoding, allowing the model to account for systematic differences in postprandial responses among participants with repeated meal observations. The continuous target was standardized within the modeling pipeline before model fitting and was transformed back to its original scale when predictions were generated.

Two nonlinear regression algorithms were evaluated for T1: support vector regression (SVR) [17] and kernel ridge regression (KRR), both using a radial basis function (RBF) kernel. The optimized RBF-SVR model was designated as the primary T1 model, and the optimized RBF-KRR model was evaluated as a candidate model. A prespecified weighted ensemble was evaluated as a secondary model.

Pipeline 2: Positive iAUC Regression. T2, the positive iAUC, was modeled without including the participant identifier. Predictions therefore depended on measured baseline clinical characteristics, pre-meal glucose information, and meal macronutrient composition rather than explicit participant-identity encoding. Because continuous clinical and meal-composition predictors could contain extreme values, these features were transformed using robust scaling based on their medians and interquartile ranges.

The T2 response was transformed within the modeling pipeline using a Yeo-Johnson power transformation and was returned to its original scale during prediction [18]. The Yeo-Johnson transformation was applied to reduce skewness in the nonnegative T2 distribution and accommodate zero-valued observations. A degree-2 polynomial KRR model was designated as the primary T2 model, and Bayesian ridge regression was evaluated as a candidate model. A fixed-weight ensemble combining the polynomial KRR prediction and the Bayesian ridge prediction was evaluated as a secondary model.

Pipeline 3: Continuous GRTB-4h Regression. T3, the continuous GRTB-4h outcome, was modeled using the same participant-identifier-free preprocessing framework as T2. The participant identifier was excluded, continuous predictors were transformed using robust scaling, and the continuous GRTB-4h outcome was transformed using the Yeo-Johnson procedure before model fitting. A degree-2 polynomial

KRR model was designated as the primary T3 model, Bayesian ridge regression was evaluated as a candidate model, and a fixed-weight ensemble combining the polynomial KRR prediction and the Bayesian ridge prediction was evaluated as a secondary model. As defined in Section 2.2, this regression pipeline included only meals with an observed GRTB-4h value. Meals without an observed qualifying recovery by four hours were not assigned an artificial continuous recovery time and were excluded from this pipeline.

Pipeline 4: Delayed-Recovery Classification. T4 classified meals according to whether glucose returned to the defined recovery threshold within two hours of meal ingestion. The participant identifier was excluded from this pipeline, and continuous predictors were transformed using robust scaling. Because T4 was binary, no continuous-target transformation was applied. Logistic regression and a support vector classifier with an RBF kernel were evaluated as candidate classification algorithms. Model hyperparameters, including regularization strength and the use of class weighting, were optimized within the training data. For the RBF support vector classifier, the kernel coefficient was also optimized. The classifier with the higher cross-validated area under the receiver operating characteristic curve within the training data was designated as the primary T4 model. Predicted probabilities were converted to class predictions using a threshold of 0.50.

The T4 classification pipeline included meals that reached the defined recovery threshold within two hours, meals that reached the threshold between two and four hours, and meals that had not reached the threshold by four hours. The latter two groups were assigned to the delayed-recovery class because the available CGM data established that the recovery threshold had not been reached within two hours. In contrast to the continuous GRTB-4h regression, this classification did not require estimation or imputation of an exact recovery time for meals without an observed recovery by four hours.

Together, these four pipelines allowed a common pool of pre-meal, meal-composition, and baseline clinical information to be evaluated against complementary measures of glucose-excursion magnitude, cumulative postprandial glucose exposure, and glucose recovery, with recovery represented using both continuous and binary outcomes. The procedures used to construct the training and holdout partitions, select predictors, optimize hyperparameters, and prevent information leakage are described in Section 2.5.

2.5 Model Training and Validation Procedure

To evaluate the outcome-specific machine learning pipelines, a chronological, within-participant holdout partition was applied separately for each target. For every eligible participant, the recorded order of meal observations was preserved. Approximately the first 90% of eligible meals were assigned to the training set, and the final 10%, with a minimum of one meal per participant, were reserved as the holdout test set. Participants with fewer than eight eligible meal observations for a given target were excluded from that target's modeling analysis. For T3, eligibility additionally required an observed GRTB-4h value within the four-hour postprandial window. For T4, meals without an observed recovery by four hours remained eligible because it was known

that the defined recovery threshold had not been reached within two hours. This minimum-meal criterion was used to permit repeated observations from each retained participant to contribute to model development while also reserving at least one later meal for chronological holdout evaluation. Only participants meeting the target-specific minimum-meal requirement contributed to the corresponding training and holdout sets; therefore, the holdout sets did not necessarily include all 12 participants in the analytic cohort. These procedures yielded holdout sets of eight meals for T1, T2, and T4 and six meals for T3.

Given the modest sample size and the number of candidate predictors, a parsimonious feature-selection strategy was used to limit model complexity and reduce the influence of redundant predictors, consistent with feature-selection approaches used in physiological machine learning [19]. Predictor selection was conducted separately for each response using forward selection within the training data. For the three continuous outcomes, ridge regression was used as a regularized surrogate estimator, and candidate predictors were evaluated using cross-validated R^2. Min-max scaling was used during T1 feature selection, whereas robust scaling was used for T2 and T3. A candidate variable was retained only when its addition improved the cross-validated R^2 beyond the prespecified improvement threshold. The minimum required improvement was 0.005 for T1 and 0.010 for T2 and T3.

For the binary T4 outcome, feature selection was performed using logistic regression as the surrogate classifier. Candidate predictors were evaluated using repeated stratified cross-validation, with the area under the receiver operating characteristic curve (ROC-AUC) as the selection criterion. A candidate predictor was retained only when it increased the cross-validated ROC-AUC by more than 0.010. This classification-specific procedure ensured that T4 predictor selection was based on discrimination between timely and delayed recovery rather than on a continuous-outcome metric.

After feature selection, model hyperparameters were optimized within the training data using grid search. For T1-T3, the grid search used five-fold cross-validation repeated three times and R^2 as the optimization criterion. The RBF-SVR and RBF-KRR hyperparameters were optimized separately for T1, whereas the degree-2 polynomial KRR and Bayesian ridge hyperparameters were optimized separately for T2 and T3. The secondary fixed-weight ensembles described in Section 2.4 were constructed from the optimized component-model predictions and were not assigned data-derived ensemble weights.

For T4, logistic regression and RBF support vector classification were optimized using repeated stratified cross-validation and ROC-AUC. The number of folds was set to five when supported by the number of observations in the smaller training class. Regularization strength and class weighting were evaluated for both classifiers, and the RBF kernel coefficient was additionally optimized for the support vector classifier. The classifier with the higher cross-validated training ROC-AUC was designated as the primary T4 model.

Target-specific handling was applied only within the training data. For T1, the training outcome was winsorized at its 1st and 99th percentiles to reduce the influence of extreme glucose-excursion values during model fitting. The corresponding

holdout observations were not winsorized. T2 and T3 were not clipped before model fitting because their Yeo-Johnson transformations were applied within their respective pipelines. T4 was retained as its original binary coding and was not transformed.

All model-based scaling and target transformations were estimated from the training data and subsequently applied to the holdout observations. Hyperparameter selection and primary-model designation were completed without using holdout outcomes. After prediction, T1 estimates were constrained to values of at least -5 mg/dL, T2 estimates were constrained to non-negative values, and T3 estimates were bounded between 0 and 240 minutes. For T4, predicted probabilities of delayed recovery were converted to class predictions using a threshold of 0.50.

The resulting holdout predictions were used only for the final evaluation of predictive performance. The regression and classification metrics used for this evaluation are described in Section 2.6.

2.6 Evaluation and Metrics

Predictive performance was evaluated using the holdout meals reserved through the within-participant partition described in Section 2.5. Metrics were calculated separately for every evaluated algorithm. Results from the designated primary model were emphasized, while the candidate and secondary models were retained for comparison.

For the three continuous outcomes, predictive accuracy was evaluated using mean absolute error (MAE), root mean squared error (RMSE), and the coefficient of determination (R^2). MAE quantified the average absolute difference between the predicted and observed outcomes in their original units: mg/dL for T1, mg/dL·min for T2, and minutes for T3. RMSE was reported in the same outcome-specific units but assigned greater weight to larger prediction errors. The R^2 statistic quantified model performance relative to a constant reference model that predicts the mean observed outcome in the holdout set. Higher R^2 values indicated better predictive performance, whereas negative values indicated performance below that reference.

The direction of prediction error was also evaluated for each continuous target. Signed error was defined as the predicted value minus the observed value. A positive signed error was classified as an overestimation, a negative signed error as an underestimation, and a signed error equal to zero within numerical tolerance as an exact prediction. Mean and median signed errors were used to characterize the overall direction of prediction error. The mean magnitude of overestimation was calculated among overestimated meals, and the mean absolute magnitude of underestimation was calculated among underestimated meals.

For the binary T4 outcome, discrimination was evaluated using ROC-AUC. This metric assessed the ability of the predicted probabilities to distinguish meals that did not reach the defined recovery threshold within two hours from meals that reached the threshold within two hours. Holdout ROC-AUC was calculated only when both recovery classes were represented in the holdout set.

Classification performance was additionally evaluated using accuracy, balanced accuracy, specificity, precision, recall, and the F1 score. Failure to reach the defined recovery threshold within two hours was treated as the positive class, whereas reaching

the threshold within two hours was treated as the negative class. Accordingly, specificity represented the proportion of meals that reached the threshold within two hours that were correctly identified. Precision represented the proportion of meals predicted to have delayed recovery that were truly in the delayed-recovery class.

All metrics were calculated using the observed holdout outcomes in their original form and the post-processed predictions described in Section 2.5.

2.7 Software and Computational Environment

Data processing and machine learning analyses were conducted in Python version 3.13.9. Data manipulation and numerical computations used pandas version 2.3.3, NumPy version 2.3.5, and SciPy version 1.16.3. Machine learning models were implemented using scikit-learn version 1.7.2.

2.8 Use of a Large Language Model

ChatGPT (OpenAI) was used during manuscript preparation to assist with language refinement, manuscript organization, and revision of manuscript text. The authors reviewed and edited all AI-assisted text and take full responsibility for the scientific content and accuracy of the final manuscript.

Code availability

The code used for data preprocessing and model development is available from the corresponding author upon reasonable request.

3 Results

The following section presents the characteristics of the analytic dataset, the predictors selected for each outcome, and the holdout performance of the outcome-specific models.

3.1 Dataset and Baseline Demographic and Clinical Characteristics

Of the 21 participants initially available for the present secondary analysis, 12 contributed meal events that remained eligible after meal-CGM alignment and application of the prespecified signal-quality criteria. The final meal-level analytic dataset therefore comprised $N = 109$ eligible meal events from these 12 participants, each associated with a six-hour observation window spanning the two hours preceding and the four hours following meal ingestion. The baseline demographic and clinical characteristics of the analytic cohort are presented in Table 1. At baseline, the mean HbA1c was 6.0 $\pm$ 0.3%, the mean two-hour OGTT glucose concentration was 196.2 $\pm$ 64.2 mg/dL, and the mean PBF was 41.5 $\pm$ 9.2%.

3.2 Selected Predictors Across Outcomes

Following the forward-selection procedure, a parsimonious predictor set was identified separately for each outcome. For the acute glucose excursion (T1), the final predictor set comprised glucose at meal initiation, digestible carbohydrates, baseline two-hour OGTT glucose, and the carbohydrate-to-fiber ratio. For the positive iAUC outcome (T2), the retained predictors were glucose at meal initiation, digestible carbohydrates, baseline PBF, baseline two-hour OGTT glucose, total fat, and the protein-to-carbohydrate ratio. For the continuous GRTB-4h outcome (T3), the final predictor set included glucose at meal initiation, digestible carbohydrates, and baseline two-hour OGTT glucose. The same three predictors were retained for the binary delayed-recovery outcome (T4).

Across the four outcomes, glucose at meal initiation, digestible carbohydrates, and baseline two-hour OGTT glucose were common to all final predictor sets. The carbohydrate-to-fiber ratio was additionally retained for T1, whereas PBF, total fat, and the protein-to-carbohydrate ratio were additionally retained for T2.

3.3 Predictive Performance of the Continuous Outcomes

Predictive performance for the three continuous outcomes was evaluated using the chronological within-participant holdout meals described in Section 2.5. Table 2 summarizes the holdout performance of the primary, candidate, and secondary models. Primary-model designation was based exclusively on training-set cross-validation and was completed without reference to holdout performance.

For T1, the primary RBF-SVR model achieved an MAE of 13.12 mg/dL, an RMSE of 17.11 mg/dL, and an R^2 of 0.78. For T2, the primary polynomial KRR model achieved an MAE of 2659.93 mg/dL·min, an RMSE of 3520.33 mg/dL·min, and an R^2 of 0.65 for positive iAUC. Although Bayesian ridge regression produced a lower holdout MAE for T2, the polynomial KRR model remained the designated primary model because model selection was based on training-set cross-validation rather than holdout performance. For T3, the primary polynomial KRR model produced an MAE of 52.04 min, an RMSE of 61.67 min, and an R^2 of 0.27 among meals with an observed qualifying recovery. The holdout R^2 was highest for acute glucose excursion, followed by positive iAUC, and was lower for continuous GRTB-4h.

Figure 1 presents the observed and predicted values from the designated primary models. The dashed diagonal line represents perfect agreement between observed and predicted values.

The direction of prediction error differed across the three continuous outcomes. For T1, overestimation occurred for 75% of predictions, whereas underestimation occurred for 25%. The mean and median signed errors were 7.42 and 5.62 mg/dL, respectively. Among overestimated meals, the mean magnitude of overestimation was 13.70 mg/dL, whereas the mean absolute magnitude of underestimation among underestimated meals was 11.39 mg/dL.

For T2, overestimation occurred for 75% of predictions, whereas underestimation occurred for 25%. The mean signed error was −231.54 mg/dL·min, whereas the median signed error was 558.78 mg/dL·min. The mean magnitude of overestimation

was 1618.93 mg/dL·min, compared with a mean absolute underestimation magnitude of 5782.93 mg/dL·min. Thus, although overestimation occurred more frequently, the larger errors among the underestimated meals resulted in a slightly negative mean signed error.

For T3, underestimation occurred for 66.67% of predictions, whereas overestimation occurred for 33.33%. The mean and median signed errors were −19.62 and −27.19 min, respectively. The mean magnitude of overestimation was 48.63 min, whereas the mean absolute magnitude of underestimation was 53.75 min. Overall, overestimation occurred more frequently for T1 and T2, whereas continuous GRTB-4h was more frequently underestimated.

3.4 Glucose Recovery Patterns

Four-hour glucose-recovery status was evaluable for all 109 meal events. Within the four-hour postprandial observation window, 84 meals (77.06%) reached the defined recovery threshold, whereas no qualifying recovery was observed for the remaining 25 meals (22.94%). Categorization according to recovery timing showed that 39 meals (35.78%) reached the recovery threshold within two hours, 45 meals (41.28%) reached the threshold between two and four hours, and 25 meals (22.94%) had not reached the threshold by four hours. Consequently, 64.22% of meals either required more than two hours to reach the recovery threshold or did not exhibit an observed qualifying recovery during the four-hour window, providing the descriptive basis for the delayed-recovery class evaluated as T4.

Among meals with an observed qualifying recovery, the mean GRTB-4h was 120.70 min (standard deviation [SD], 66.94), with a median of 132.55 min and a range of 5.27-233.28 min. Meals that reached the recovery threshold within two hours, by definition, required no additional recovery time beyond the 120-minute threshold. Among meals that reached the recovery threshold between two and four hours, the mean additional recovery time beyond this threshold was 53.91 min (SD, 31.28), with a median of 53.93 min and a range of 2.53-113.28 min. Meals without an observed qualifying recovery by four hours were not assigned an artificial continuous recovery time and were excluded from these continuous-time summaries. The recovery categories and additional recovery times are presented in Figure 2.

3.5 Classification of Delayed Glucose Recovery

T4 evaluated whether meals that did not reach the defined recovery threshold within two hours could be distinguished from those that reached the threshold within two hours. The RBF support vector classifier (RBF-SVC) was designated as the primary model during model development. In the chronological within-participant holdout evaluation, the RBF-SVC achieved a higher ROC-AUC than logistic regression, whereas both models produced identical classifications at the prespecified probability threshold of 0.50. Complete holdout performance results are presented in Table 3.

The primary RBF-SVC achieved a holdout ROC-AUC of 0.83, compared with 0.75 for logistic regression. Both models produced the same accuracy, balanced accuracy, specificity, precision, recall, and F1 score at the 0.50 classification threshold. Thus,

the difference in ROC-AUC reflected differences in probability-based discrimination rather than differences in the final binary classifications at the prespecified threshold.

4 Discussion

This study evaluated complementary dimensions of the postprandial glucose response using four outcome-specific predictive models. Acute glucose excursion and positive iAUC achieved holdout R^2 values of 0.78 and 0.65, respectively. The delayed-recovery classifier achieved a holdout ROC-AUC of 0.83, whereas continuous GRTB-4h achieved a holdout R^2 of 0.27. These differences indicate that postprandial response magnitude, cumulative glucose exposure, and recovery time capture related but distinct aspects of glycemic regulation and differ in the extent to which they can be predicted from meal composition, baseline clinical characteristics, and pre-meal glucose information.

These dimensions are related but not interchangeable. Acute glucose excursion reflects the maximum increase above the glucose concentration at meal initiation. Positive iAUC characterizes cumulative glucose exposure above the glucose concentration at meal initiation, extending until the first return to that concentration or up to four hours when it was not reached. GRTB-4h captures a different characteristic by quantifying the time from meal ingestion until the first qualifying post-peak recovery. The differences in predictive performance indicate that accurately estimating the magnitude or cumulative exposure of a postprandial response does not necessarily imply equally accurate estimation of recovery time. Previous precision-nutrition studies have similarly demonstrated marked inter-individual variability in postprandial responses and shown that combining meal characteristics with host information can support individualized prediction [6–8, 10, 20]. The present study extends this framework by jointly evaluating acute excursion, cumulative exposure, and recovery time in adults with prediabetes rather than representing the postprandial response using a single summary outcome.

The outcome-specific predictor patterns further illustrate these differences. Glucose at meal initiation, digestible carbohydrates, and baseline two-hour OGTT glucose were retained across all four outcomes, indicating that both the immediate glycemic state and information related to meal carbohydrate exposure and glucose tolerance contributed predictive information across different components of the postprandial response. The carbohydrate-to-fiber ratio was additionally retained for acute glucose excursion. Positive iAUC retained a broader predictor set that additionally included baseline PBF, total fat, and the protein-to-carbohydrate ratio. In contrast, the continuous GRTB-4h and binary delayed-recovery outcomes retained the same three predictors: glucose at meal initiation, digestible carbohydrates, and baseline two-hour OGTT glucose. These differences suggest that the information useful for predicting cumulative postprandial exposure may not be identical to that required for predicting the magnitude or timing of glucose recovery. However, these variables were selected for their incremental predictive value within the present dataset and should not be interpreted as independent or causal determinants of the corresponding outcomes.

The recovery analyses further demonstrated the value of representing postprandial recovery using both continuous and binary outcomes. Within the four-hour observation window, 77.06% of meals reached the defined recovery threshold, including 35.78% within two hours and 41.28% between two and four hours, whereas no qualifying recovery was observed by four hours for 22.94% of meals. Continuous GRTB-4h therefore characterized observed recovery time only for meals in which the defined threshold was reached within the observation window. T4 provided a complementary representation by distinguishing meals that reached the recovery threshold within two hours from those that did not. Meals without an observed qualifying recovery by four hours could therefore remain informative for the binary delayed-recovery outcome without assigning them an artificial continuous recovery time. This distinction preserves the observed information available for each meal while avoiding imputation of an exact recovery time that was not measured.

The delayed-recovery classifier achieved a holdout ROC-AUC of 0.83, although its threshold-dependent classification metrics were more modest. Given the small holdout sample, these findings should be interpreted as exploratory rather than as evidence that categorical recovery is inherently easier to predict.

The lower predictive performance for continuous GRTB-4h compared with acute excursion and positive iAUC may reflect differences in the information captured by these outcomes. Acute excursion reflects the maximum glucose rise above baseline, whereas positive iAUC integrates both the magnitude and duration of glucose elevation across the postprandial trajectory. In contrast, GRTB-4h is a temporal measure determined by the time required for glucose to reach a prespecified post-peak recovery threshold. It may therefore be influenced by variability across the entire postprandial trajectory, including the rate of glucose rise, time to peak, and rate of subsequent decline toward baseline. The comparatively lower R^2 for GRTB-4h should therefore not necessarily be interpreted as indicating lower physiological relevance, but rather that recovery time may be influenced by factors not fully captured by the available predictors.

The direction-of-error analysis provided additional information beyond aggregate measures of predictive performance. Acute glucose excursion and positive iAUC were more frequently overestimated than underestimated, whereas continuous GRTB-4h was more frequently underestimated. For positive iAUC, the mean signed error was slightly negative despite the greater frequency of overestimation because the magnitude of the underestimation errors was substantially larger. This pattern illustrates why the frequency and magnitude of directional errors should be considered together when evaluating model behavior. For continuous GRTB-4h, the predominance of underestimation indicates that the model more often predicted recovery earlier than was observed in the holdout meals. These results are descriptive and require confirmation in larger datasets before systematic prediction tendencies can be established.

Several limitations should be considered when interpreting these findings. The final analytic dataset comprised 109 meal events from 12 participants, which limits the power of the study and generalizability of the predictive results. Repeated meal observations provide substantial meal-level information but do not provide the

same independent information as a larger number of participants, particularly for participant-level characteristics such as HbA1c, OGTT glucose, PBF, and DLM. In addition, independent participant-level validation in a larger cohort will be necessary to assess generalizability. Accordingly, the present findings should be interpreted as exploratory feasibility results intended to inform subsequent validation in larger and independent cohorts. This framing is consistent with prior small, intensively sampled CGM investigations that were explicitly presented as pilot or exploratory feasibility studies [11, 21].

The relatively small dataset also limited the complexity of the models and the ability to investigate higher-order interactions without increasing the risk of overfitting. The performance estimates obtained from the small holdout sets should therefore be interpreted as exploratory rather than as precise estimates of clinical predictive performance. Moreover, because the chronological holdout observations were obtained from participants whose earlier meals contributed to model development, the present evaluation assesses temporal within-participant prediction rather than generalization to previously unseen participants. Independent participant-level validation in a larger cohort will therefore be required before the predictive performance of these models can be established more definitively. This consideration is particularly important for continuous recovery time, for which eligibility required an observed qualifying recovery within the four-hour window. The resulting GRTB-4h model therefore applies specifically to meals with an observed recovery and does not estimate an exact recovery time for meals that remained above the recovery threshold at four hours.

Additional limitations arise from the free-living measurement environment. CGM measures interstitial rather than plasma glucose, and physiological lag between these compartments may affect the estimated timing of glucose peaks and recovery [22]. Food records are subject to uncertainty in reported meal timing, portion size, and nutrient composition. Other contextual factors not included in the present models, including physical activity and sleep, may also influence postprandial glucose responses [23], while stress may independently alter glucose dynamics [11]. Preceding meals and meal sequence were likewise not explicitly modeled and may contribute additional variability. Future studies incorporating larger and more diverse cohorts, participant-level external validation, standardized meal challenges, and additional behavioral and physiological information will be important for determining the stability, transportability, and potential clinical utility of these predictive approaches.

Taken together, the findings support modeling postprandial glucose excursion, cumulative exposure, and recovery as related but distinct components of the glycemic response. Acute glucose excursion and positive iAUC were predicted with higher holdout R^2 values than exact GRTB-4h, while delayed-recovery classification provided a complementary categorical representation of the recovery process. The differences in selected predictors and predictive performance across these outcomes reinforce the value of evaluating multiple dimensions of postprandial glycemia rather than relying on a single summary measure. Larger and independent cohorts will be necessary to determine whether these patterns generalize and whether multidimensional prediction can ultimately contribute to individualized nutrition strategies.

5 Conclusions

This study supports a multidimensional framework for evaluating postprandial glucose responses in adults with prediabetes using baseline clinical characteristics, pre-meal glucose information, and meal composition. Chronological within-participant hold-out evaluation showed higher predictive performance for acute glucose excursion and positive iAUC than for continuous GRTB-4h, while delayed-recovery classification provided a complementary categorical representation of the recovery process. Together, these findings indicate that response magnitude, cumulative postprandial glucose exposure, and recovery represent distinct but complementary dimensions of postprandial glycemic regulation. The differences in predictive performance and selected predictors across these outcomes further support evaluating multiple aspects of the postprandial response rather than relying on a single summary measure. Validation in larger and independent cohorts will be necessary to determine the generalizability and potential clinical utility of this framework for future individualized nutrition approaches.

Declarations

Funding

This research received no external funding.

Ethics approval and consent to participate

The parent trial was conducted in accordance with the Declaration of Helsinki and was approved by the George Mason University Institutional Review Board. The present secondary analysis was reviewed and determined to be exempt. Informed consent was obtained from all participants enrolled in the parent trial.

Consent for publication

Not applicable.

Materials availability

Not applicable.

Data availability

The data supporting the findings of this study are available from the corresponding author upon reasonable request. Requests should be directed to `rbasiri@gmu.edu`.

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Author contributions

Conceptualization: R.B.; methodology: R.B., J.W., and M.B.; software: R.B. and M.B.; validation: R.B., J.W., and G.H.; formal analysis: M.B.; investigation: R.B., J.W., and M.B.; resources: R.B., J.W., and G.H.; data curation: R.B. and M.B.; writing—original draft preparation: M.B.; writing—review and editing: R.B., J.W., and G.H.; visualization: M.B.; supervision: R.B., J.W., and G.H.; project administration: R.B.

Additional Information

Competing interests

The authors declare no competing interests.

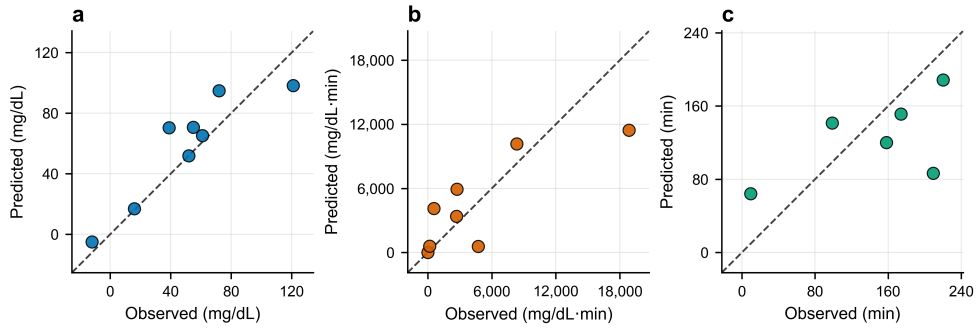


Fig. 1 Observed versus predicted values for the primary continuous-outcome models in the chronological within-participant holdout sets. **(a)** Acute glucose excursion predicted using RBF support vector regression (MAE = 13.12 mg/dL; RMSE = 17.11 mg/dL; R^2 = 0.78). **(b)** Positive iAUC predicted using polynomial kernel ridge regression (MAE = 2659.93 mg/dL·min; RMSE = 3520.33 mg/dL·min; $R^2 = 0.65$). **(c)** Continuous GRTB-4h predicted using polynomial kernel ridge regression among meals with an observed qualifying recovery (MAE = 52.04 min; RMSE = 61.67 min; R^2 = 0.27). Each point represents one holdout meal. The dashed diagonal line represents perfect agreement; points above the line indicate overestimation, whereas points below the line indicate underestimation.

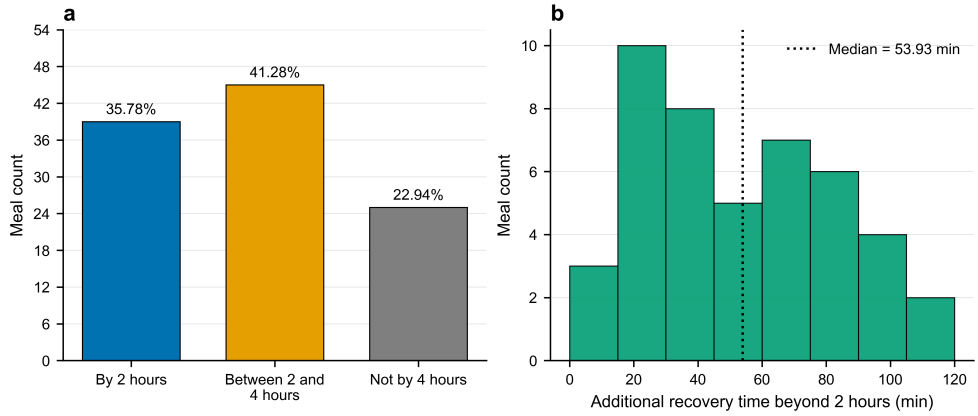


Fig. 2 Postprandial glucose recovery patterns during the four-hour observation window. **(a)** Distribution of meals according to whether glucose reached the defined recovery threshold, at or below 5 mg/dL above the glucose concentration at meal initiation, within two hours, between two and four hours, or had not reached the threshold by four hours. Percentages were calculated relative to all evaluable meal events. **(b)** Distribution of the additional recovery time beyond two hours among meals with an observed qualifying recovery between two and four hours. The dotted vertical line indicates the median additional recovery time of 53.93 min. Meals without an observed qualifying recovery by four hours were not assigned an artificial continuous recovery time and were not included in the continuous recovery-time distribution.

Table 1 Baseline demographic and clinical characteristics of the analytic cohort.

Characteristic	**Analytic cohort** ($N = 12$)
Age, years (mean ± SD)	56.7 ± 6.6
Sex, *n* (%)	
Female	8 (66.7)
Male	4 (33.3)
Race, *n* (%)	
White	8 (66.7)
Asian	3 (25.0)
Black/African American	1 (8.3)
BMI, kg/m^2 (mean ± SD)	31.6 ± 4.1[1]
HbA1c, % (mean ± SD)	6.0 ± 0.3
Two-hour OGTT glucose, mg/dL (mean ± SD)	196.2 ± 64.2
Percent body fat, % (mean ± SD)	41.5 ± 9.2
Dry lean mass, kg (mean ± SD)	13.4 ± 3.9

SD, standard deviation; BMI, body mass index; HbA1c, glycated hemoglobin; OGTT, oral glucose tolerance test.

[1]Baseline BMI was available for 11 of the 12 participants.

Table 2 Holdout performance of the models evaluated for the three continuous outcomes. Primary models, designated using training-set cross-validation without reference to holdout performance, are shown in bold.

Outcome	Model	MAE	RMSE	R^2
T1 $n_{\text{train}} = 81,\ n_{\text{test}} = 8$	**RBF-SVR**	13.12	17.11	0.78
	RBF-KRR	16.47	19.49	0.72
	Fixed ensemble	13.96	17.52	0.77
T2 $n_{\text{train}} = 81,\ n_{\text{test}} = 8$	**Polynomial KRR**	2659.93	3520.33	0.65
	Bayesian ridge	2219.36	3743.20	0.60
	Fixed ensemble	2459.89	3551.86	0.64
T3 $n_{\text{train}} = 59,\ n_{\text{test}} = 6$	**Polynomial KRR**	52.04	61.67	0.27
	Bayesian ridge	52.91	62.55	0.25
	Fixed ensemble	52.39	61.89	0.26

T1, acute glucose excursion (mg/dL); T2, positive incremental area under the glucose curve (mg/dL·min); T3, continuous glucose recovery time to baseline within four hours (GRTB-4h; min); MAE, mean absolute error; RMSE, root mean squared error; RBF, radial basis function; SVR, support vector regression; KRR, kernel ridge regression. Sample sizes indicate the numbers of meal observations used for model training and chronological holdout evaluation after application of the target-specific eligibility criteria.

Table 3 Holdout performance of the models evaluated for classification of delayed glucose recovery. The designated primary model is shown in bold.

Model	ROC-AUC	Acc.	Bal. Acc.	Spec.	Prec.	Recall	F1
RBF-SVC	0.83	0.63	0.58	0.50	0.80	0.67	0.73
Logistic regression	0.75	0.63	0.58	0.50	0.80	0.67	0.73

Failure to reach the defined recovery threshold within two hours was treated as the positive class, whereas reaching the threshold within two hours was treated as the negative class. The recovery threshold was defined as the first qualifying post-peak CGM reading at or below 5 mg/dL above the glucose concentration at meal initiation. Meals without an observed qualifying recovery by four hours remained in the delayed-recovery class because the available CGM data established that the recovery threshold had not been reached within two hours. Predicted probabilities were converted to class predictions using a threshold of 0.50. ROC-AUC, area under the receiver operating characteristic curve; Acc., accuracy; Bal. Acc., balanced accuracy; Spec., specificity; Prec., precision; CGM, continuous glucose monitoring; RBF, radial basis function; SVC, support vector classifier.