Differential impact of lifestyle factors on 2-hour glucose values in individuals with type 2 diabetes: potential for more personalized interventions

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Differential impact of lifestyle factors on 2-hour glucose values in individuals with type 2 diabetes: potential for more personalized interventions

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ABSTRACT

Introduction Lifestyle determinants of 2-hour glucose concentration in people with type 2 diabetes and interindividual differences need to be identified.

Research design and methods 38 participants with type 2 diabetes, treated with lifestyle advice and/or metformin, tracked their physical activity, sleep and dietary intake, while continuously monitoring interstitial glucose concentrations for 11 periods of four consecutive days each. A linear mixed-effects model was used to quantify the effect of sleep, stress, current glucose, carbohydrate intake and exercise on glucose levels 2 hours later.

Results The final model identified carbohydrate intake (grams) in the past 5 min as well as in the past 30 min, sleep duration during the previous night (hours) and physical activity (metabolic equivalents) over the past 12 hours as significant fixed effects that influenced glucose concentrations 2 hours later. In addition, carbohydrate intake in the past 5 and past 30 min, and physical activity in the past and future 30 min were included as random or individualized effects. Although carbohydrate intake led to increased glucose concentrations in 2 hours in all individuals, the magnitude of this effect varied between individuals. The physical activity on glucose concentrations in 2 hours varied among individuals as well, in terms of magnitude and in terms of direction (showing either increase or decline).

Conclusions Carbohydrate intake, sleep and physical activity at specific points in time have both fixed as well as individualized effects on glucose concentrations 2 hours later in individuals with type 2 diabetes. Interindividual differences in glycemic response to lifestyle components call for personalized advice in the management of type 2 diabetes.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Carbohydrates and exercise can affect people with type 2 diabetes differently as shown in clinical trials.

WHAT THIS STUDY ADDS

⇒ During daily living the effect of exercise and carbohydrate is shown to differ.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ This study indicated that lifestyle should be personalized when it comes to carbohydrate consumption and exercise for people with diabetes treated with lifestyle only or only with metformin.

INTRODUCTION

Type 2 diabetes is a metabolic disorder that affects millions of individuals worldwide.[1] Lifestyle modification, including changes in dietary intake and physical activity, is widely recommended as a primary treatment approach.[2] Indeed, adopting a healthy lifestyle can enhance insulin sensitivity and improve glycemic control.[3] Personalization of lifestyle advice, taking into account the person's biological, cultural, social, and economic background may facilitate long-term engagement and optimal health outcomes.[4–6] As the effect of distinct lifestyle factors on blood glucose concentrations may vary substantially among individuals, personalized advice should ideally take into account the individualized glucose response to lifestyle.[7] For example, the postprandial glucose response to identical meals was highly variable among individuals in an 800-person cohort of people without diabetes.[8] Also, the glycemic response to a starch-rich meal was reported to vary substantially between and within 10 individuals with type 2 diabetes, and 50 min of walking before dinner increased postprandial glucose concentrations in some and reduced them in others in a group of 80 people with type 2 diabetes.[8–11]

Providing personalized lifestyle advice requires knowledge of how different lifestyle components affect glucose regulation per se, as well as knowledge on interindividual variation therein. Important components to incorporate in a lifestyle intervention for type 2 diabetes are physical activity, dietary intake and sleep.[2] The impact of these lifestyle

components on glycemic control in patients with type 2 diabetes has been well studied in highly controlled research settings.[12–18] However, studies under such controlled conditions, often focusing on the impact of specific lifestyle components in isolation, may not fully capture the effects of lifestyle, or the interaction between distinct components, on glucose control in daily life. We used a variety of sensors and apps to monitor dietary intake, physical activity, sleep and glucose concentrations in people with type 2 diabetes in real life. Subsequently, a linear mixed-effects model was used to determine which of these lifestyle features, within prespecified time frames, had the greatest impact on glucose concentrations 2 hours later. The selection of the 2-hour time point as an outcome measure is underpinned by two key considerations. First, prediction of glucose levels at a time point 2 hours in the future provides people with type 2 diabetes with a reasonable amount of time for proactive intervention, if such prediction algorithms were included in an application for real-time feedback in a real-life setting. Second, the 2-hour glucose level is used in oral glucose tolerance tests as a diagnostic criterion. Generally speaking, 2 hours should be enough for postprandial glucose levels to return to normal in a healthy person and as such provides insight into whether glucose concentrations normalize within a clinically desirable time window, rather than trying to predict a temporary peak in glucose. That renders it an optimal interval for assessing the putative effects of dietary intake, physical activity and/or sleep on glucose concentrations. We used a linear mixed-effects model because it is fully explainable and can conveniently identify significant individualized effects on top of a population average.

RESEARCH DESIGN AND METHODS

Study population and design

A total of 41 individuals with type 2 diabetes were included in the study during October 2019 and January 2021 via local newspapers and social media. Eligibility criteria required subjects to have a body mass index (BMI) below 40 kg/m^2, and no previous insulin treatment, instead relying on lifestyle modifications and/or metformin.[19] Included participants wore a continuous glucose monitor (CGM) and activity/sleep tracker, and logged their dietary intake in a food diary application (see below) during 11 monitoring periods of four consecutive days each. All monitoring periods were separated by a washout period of at least 1 week. During three of the 11 periods, participants monitored lifestyle and glucose parameters during regular daily life. These three monitoring periods, which were scheduled at study start, mid-term and end, served as control. In between control periods, participants were allocated to four distinct interventions twice, in random order. These interventions were: (1) a carbohydrate-restricted (<100 g/day) diet; (2) a Mediterranean diet; (3) 15 min of moderate-intensity walking after each main meal; and (4) 5 min of moderate-intensity physical activity every hour from 09:00 hours to 17:00 hours. At baseline, the Pittsburgh Sleep Quality Index (PSQI) questionnaire was administered as well as general characteristics.[20]

Of the 41 people with type 2 diabetes enrolled in the study, two dropped out halfway through: one due to recurring technical difficulties with the CGM and one due to a change in medication. A third participant was excluded from the data analysis due to regular night shift work. Missing data were left out of the analysis. The particulars of participant recruitment and the experimental design have been described elsewhere.[19]

Measurements and data preprocessing

The outcome variable was the glucose concentration, quantified at any point in time. The interstitial glucose concentration in millimoles per liter was measured every 5 min with the Dexcom G6 continuous glucose monitoring system (DexCom, San Diego, USA). Measured lifestyle factors included physical activity, sleep duration and dietary intake. Physical activity level was expressed in 'metabolic equivalent of task', or MET, averaged per 5 min, and sleep duration in hours per night. Both variables were measured and calculated by the Fitbit Charge 3 (Fitbit, San Francisco, USA). Dietary intake and macronutrient composition data in grams were collected using a custom smartphone application (HowAmI app, TNO, Leiden, The Netherlands) and the FatSecret database (Secret Industries, Victoria, Australia). Meal logging was done via manual entry. The nutritional information of the meals that were provided during the diet phases was already prefilled. Subject only needed to adjust the amount they consumed. In our models, we included data from 06:00 hours until 24:00 hours to capture the dynamics during waking hours. We created a suitable dataset for the prediction of glucose 2 hours in the future via data aggregation and feature engineering steps. This was done to deal with varying sampling intervals across the different modalities. The various time lags chosen were based on literature. We tried various time lags for the effect of exercise ranging from total exercise in the past 24 hours to 2 hours before the prediction moment and time points in between.[12 13 21] For carbohydrate intake, time lags ranged from the past 12 hours, to account for an overnight effect of carbohydrate consumption on breakfast glucose levels,[18] to 2 hours before the prediction moment and time points in between.[22–25] Features for physical activity level were created by averaging the METs per minute over the predefined period. Features for carbohydrate intake were created by taking the sum of grams of carbohydrates consumed over a certain predefined period. The amounts of protein and fat were not included in the model due to the high degree of multicollinearity. While techniques to mitigate this exist, it was chosen not to do so as using such techniques would hamper the interpretability of the results.

Model

We used a linear mixed-effects model, including both population (fixed) and individual (random) effects, to quantify the effects of various lifestyle factors on glucose concentrations 2 hours later. The statistical formulation for a linear mixed-effects model, considering a continuous outcome variable y_{ij} for subject $i = 1,., N$ at time point $j = 1,., J_i$ can be presented as follows:

$$y_{ij} = \mu_i + \alpha_{ij}\beta_i + \varepsilon_{ij}$$

$$\varepsilon_{ij} \sim N(0, \sigma_{\varepsilon}^2)$$

$$\mu_i \sim N(\mu_{0,\sigma_{\mu}^2})$$

$$effect: \beta_k \sim N(\beta_0, \Sigma_{\beta})$$

$$randomeffect: \beta_{i,k} \sim N(\beta_K, \sigma_{\beta k}^2)$$

where μ_i is the intercept for individual i coming from a normal distribution with the mean μ_0 as the population mean of the intercept or baseline glucose level, and σ_{μ}^2 as the corresponding variance. α_{ij} is the vector with independent variables for individual i at a time point j with the fixed and random effects model coefficients for individual i contained in vector β_i. The fixed effect $\beta_{i,k}$ is equal to the fixed effect β_k, where k indicates the variable, with a covariance matrix Σ_{β} between the fixed effects. For a random effect for variable k, $\beta_{i,k}$ is normally distributed with mean β_k, which is equal to the fixed effect if present, and is zero if no fixed effect is present, and variance $\sigma_{\beta k}^2$. The general error ϵ_{ij} follows an independent, normal distribution with mean 0 and variance σ_{ϵ}^2.

The process of creating the linear mixed-effects model was as follows (figure 1). The 'null model' included only the current glucose concentration (t=0) and an individual intercept as independent (predictor) variables to model the glucose concentration 2 hours. The individual intercept was included in the model to account for the fact that baseline glucose concentrations differ among participants, assuming baseline glucose concentrations are normally distributed within the sample. Subsequently, several lifestyle factors were included in what was called the 'full linear mixed effect model'. These lifestyle factors were hours of sleep in the previous night, physical activity and carbohydrate intake. For physical activity and carbohydrate intake, features for various time lags around t=0, with t=0 as the moment of prediction, were included in the model. The interaction between exercise and carbohydrate intake was taken into consideration, as it is shown that postprandial exercise lowers plasma glucose concentrations.[12] This was reflected in the model as an interaction effect between carbohydrate intake in the past 30 min and the exercise in the 30 min after the time of prediction, thus reflecting postprandial exercise. Finally, the added value of including BMI, diabetes duration, age, blood pressure and gender as variables with fixed effects in the model was explored. The best model was selected based on the Akaike information criterion (AIC), Bayesian information criterion (BIC) and R^2 (data not shown), that is, the model with the lowest AIC was chosen as 'full model'.

We started with this full model that included all of the preselected features as described before, after which we took out variables one by one in a stepwise fashion. For fixed effects, we removed variables that did not have a significant effect on glucose concentrations 2 hours later using a cut-off of $p<0.05$ and selected models with a lower AIC. This resulted in the intermediate model. Then, we evaluated the effect of addition or deletion of random effects by the change in AIC, resulting in the 'final model'. The linear mixed-effects models were created using lme4 (version 1.1-29) in R (R package version 4.0.3.) using restricted maximum likelihood.

RESULTS

Study participants

38 participants were included in data analysis. The average participant had an age of 63, a BMI of 28, was treated mostly with lifestyle (39%) (for full details see online supplemental table 1). Participants in the study logged at least 80% of their required calories based on their basal metabolic rate on 1231 out of 1670 days (73%).

Model fitting

The model coefficients and goodness-of-fit measures for the null, full and final models are shown in table 1. The null model included only the current glucose and the individual as a grouping-level variable. The intraclass correlation of 0.45 indicates the proportion of variance explained by the grouping variables, in this case the individual, and further justifies the choice to add the individual as a level in the multilevel model.

The full model included the glucose value at t=0, hours of sleep in the previous night, carbohydrate intake in the last 5 min, carbohydrate intake in the last 30 min, MET in the last 30 min, MET in the last 12 hours, and MET 30 min after the current moment. The full model included non-significant fixed effects for exercise. After accounting for personal differences by the random effects of exercise,

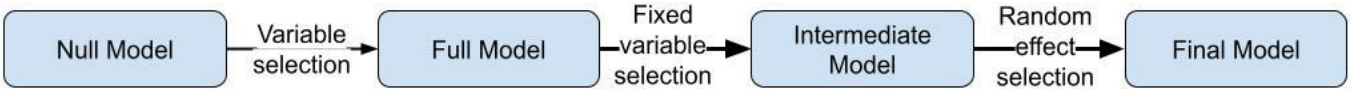

Figure 1 Flow chart of the linear mixed effects modeling approach. Starting with the null model including only the current glucose concentration and an individual intercept as independent (predictor) variables. Next, the full model included all relevant variables, where the fixed variables were removed in a stepwise manner to get to the intermediate model. Again, making a selection on the random effect to end up with the final model.

Table 1 Coefficients of the different models and goodness-of-fit measures

	Null model	Full model	Final model
Predictors	**Estimates**	**Estimates**	**Estimates**
Intercept	5.44 (4.99–5.88) **	6.03 (5.51–6.55)**	6.15 (5.69–6.61)**
Current glucose	0.35 (0.34–0.36)**	0.34 (0.33–0.36)**	0.34 (0.33–0.35)**
Sleep		−0.01 (−0.02 to −0.00)*	−0.01 (−0.02 to 0.01)*
Exercise in the past 12 hours (MET)		−0.31 (−0.35 to −0.27)**	−0.31 (−0.35 to −0.27)**
Carbohydrates in the past 5 min (g)		0.03 (0.01–0.04)**	0.02 (0.01–0.04)**
Carbohydrates in the past 30 min (g)		0.02 (0.01–0.033)**	0.02 (0.00–0.03)*
Exercise in the future 30 min (MET)		0.02 (−0.04 to 0.08)	
Exercise in the past 30 min (MET)		0.02 (−0.05 to 0.09)	
Exercise in the future 30 min (MET)×carbohydrates in the past 30 min (g)		−0.01 (−0.01 to −0.00)*	
SD of random effects			
Participant	1.376	1.57	1.62
Exercise in the future 30 min (MET)		0.16	0.16
Exercise in the past 30 min (MET)		0.2	0.2
Carbohydrates in the past 5 min (g)		0.03	0.03
Carbohydrates in the past 30 min (g)			0.04
Measures of fit			
Σ2	2.328	2.228	2.220
ICC	0.449	0.483	0.533
Marginal R^2/conditional R^2	0.136/0.523	0.137/0.554	0.127/0.592
NPAR		20	22
AIC		119580.9	119500.8
BIC		119748.9	119685.5
Deviance		119540.9	119456.8

*P<0.05, **p<0.001.
AIC, Akaike information criterion; BIC, Bayesian information criterion; ICC, intraclass correlation ; MET, metabolic equivalent of task; NPAR, number of parameters.

the fixed effects did not contribute to a better model and were therefore left out. After removing these fixed effects, the interaction effect between exercise 30 min in the future and carbohydrate intake in the past 30 min was no longer significant. Removing both this interaction effect and the fixed effects for the 30 min exercise time frame did not significantly change the other parameters and improved the model fit, justifying the choice to leave them out of the final model as well as showing the robustness of the direction of the effects.

The explained variance and model fit improved when comparing the full model with the final model. The overall quality of the final model was assessed using the AIC, BIC and R^2 (table 1). There was no strong evidence of heteroskedasticity, but the residuals were not completely normally distributed. The random effects were not normally distributed due to some individuals having a high baseline glucose concentration (online supplemental figures 1–3).

Final model results

The final model showed an R^2 of 0.124 when only considering fixed effects (marginal R^2) and 0.6 for the full model (conditional R^2). This means that taking into account individual variation, the final model explained roughly 60% of the variability in the data. The final model included four fixed effects and four random effects (figure 2). The random effects were carbohydrate intake in the past 5 and past 30 min and exercise in the past 30 and future 30 min, meaning that for these variables accounting for interindividual differences in the coefficients improved the model. The individual model coefficients of carbohydrate intake in the past 5 and 30 min were mostly positive, ranging from 0 mmol/L/g to 0.1 mmol/L/g for all but a few participants (figure 3). As seen by the Spearman correlation coefficient, the individual coefficients of carbohydrate intake are not related to baseline HbA1c levels (online supplemental figure 4). The individual coefficients for exercise were centered

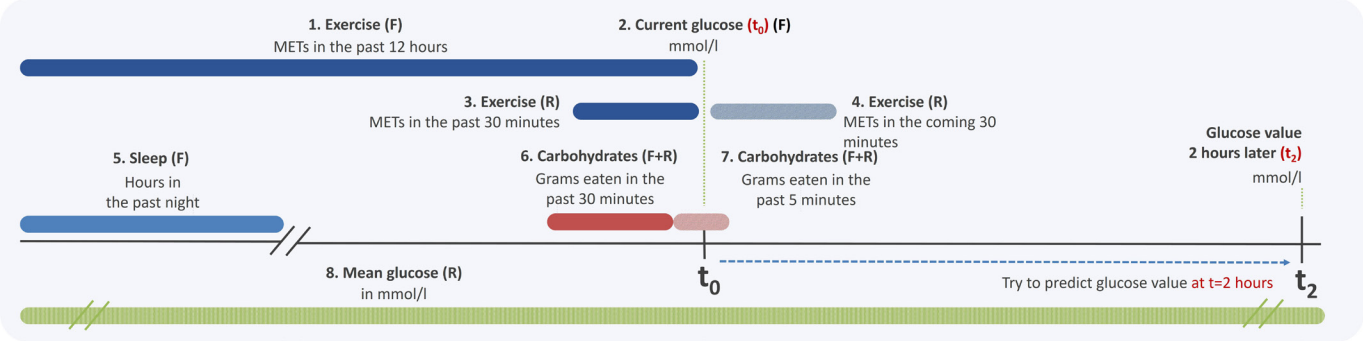

Figure 2 Predicting factors of glucose concentrations 2 hours later in the final model. F, fixed effect; MET, metabolic equivalent of task; R, random effect; t, time in hours.

around zero ranging from a negative to a positive effect on glucose concentrations 2 hours in the future, ranging from −0.5 mmol/L/MET to 0.4 mmol/L/MET (figure 3). The following fixed effects were included in the model: the current glucose in millimoles per liter, carbohydrate intake in the past 30 min and in the past 5 min in grams, sleep in the past night in hours, and activity in the past 12 hours in METs (figure 2). All fixed effects had a statistically significant effect on the glucose concentration 2 hours.

DISCUSSION

In this paper, we show that the direct effect of different lifestyle factors on glucose concentrations 2 hours later in people with type 2 diabetes during daily life can be

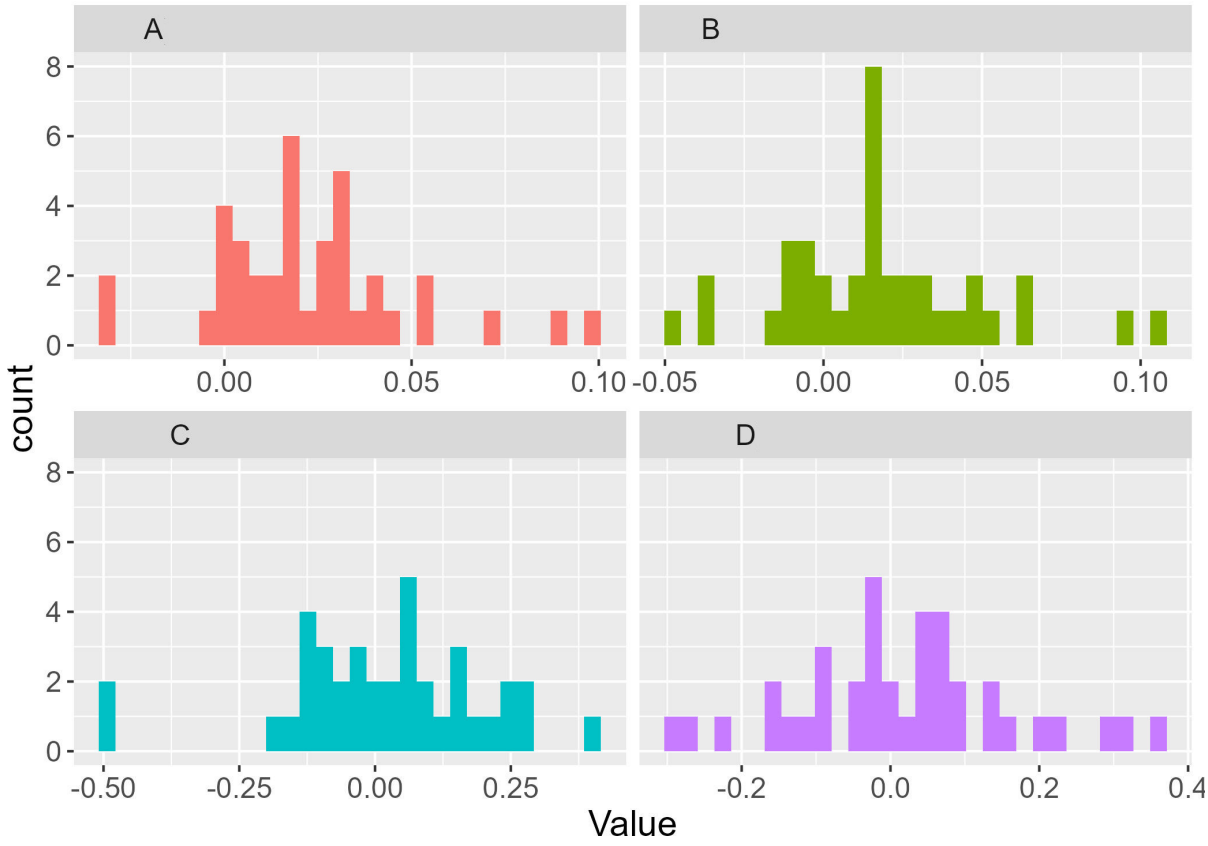

Figure 3 Individual difference in glucose response to exercise and carbohydrate as shown in a histogram depicting the distribution of individual coefficients on glucose concentrations 2 hours later. (A) Carbohydrates eaten in the last 5 min. This shows that for all but two people, carbohydrates increase the glucose concentration between 0 and 0.1 mmol/L/g of carbohydrates. (B) Similar to the carbohydrates in the last 5 min, carbohydrates eaten in the past 30 min mostly increase glucose concentration. However, the magnitude of the effect differs between individuals. (C) The effect of exercise in the last 30 min on the glucose concentrations showing both an increase and decrease in glucose concentration between individuals. (D) The effect of exercise in the next 30 min on the glucose concentrations showing again an increase and decrease in glucose concentration between individuals in response to exercise. This time, a bit larger effect than the exercise in the past 30 min.

described by a multilevel model using CGM and contextual data. The final model accounted for 60% of the variation in glucose concentrations 2 hours later as measured by a CGM.

To identify the impact of lifestyle effects on glucose concentrations for an individual, the interpretability of our model results was deemed important.[2] Limiting the included lifestyle variables to only carbohydrate intake, glucose, sleep and exercise for the sake of interpretability might limit the explained variance to some degree. For example, it is known that fat influences the gastric emptying, affecting blood glucose for over 2 hours after a meal in people with type 2 diabetes. Despite not covering all the factors that could affect glucose, our model was able to capture a significant amount of variation in the glucose concentration 2 hours later. A model using data collected in a more controlled setting, including personal characteristics and carbohydrate intake, and trying to predict a glucose peak in the next 0–4 hours accounted for 49% of the variation.[26] Potentially, by incorporating random effects into the mixed-effects model, our model could account for the inherent variability in individuals' responses, potentially including differences between individuals in protein and fat intake, and provide a more comprehensive understanding of the relationship between carbohydrate intake, exercise, sleep and 2-hour glucose concentrations.

Multilevel modeling of the 2-hour glucose concentration showed fixed effects of sleep, carbohydrate intake and exercise, and random effects for exercise and carbohydrates indicating interindividual differences in glycemic response. Overall, carbohydrate intake led to an increase in glucose concentration 2 hours later. However, the magnitude of this effect varied between individuals, with some exhibiting little to no effect and others a significant increase in glucose concentrations of up to 0.1 mmol/L for every gram of carbohydrates eaten. The fact that blood glucose concentrations increase after the consumption of carbohydrates and that the level of response varies between individuals is known,[27] but the magnitude of how much this can increase is new. The fact that the effect of carbohydrates can vary from no effect to an increase of 0.1 mmol/L/g of carbohydrates underlines the importance of looking at the individual in providing lifestyle recommendations.

The underlying cause for the large interindividual differences in glucose response to carbohydrate intake cannot be distilled by the model. Literature does provide some insights into why individuals might differ in their glucose response. First, it could be due to differences between individuals in underlying pathophysiology, such as the level of insulin resistance and which organs are mostly affected.[28 29] Second, it could be due to differences in lifestyle between individuals. It has been shown in a controlled setting that the glucose response to a specific meal is influenced by the carbohydrate content, and by the type of carbohydrate, meal composition and meal timing, and stress, and is even subject to day-to-day variation.[30–32] Lifestyle habits such as skipping breakfast, having frequent snacks or always choosing whole grains may therefore influence glycemic responses of an individual. Additionally, meal order or carry-over effects between meals could partly explain the variability in postprandial glucose response in real life.[22 26] Irrespective of the cause, the interindividual differences in glucose response to carbohydrates should be considered when interpreting glucose values for individuals with type 2 diabetes.

From our model, exercise in the past day seems to have a small but beneficial effect on glucose concentrations. This feature could represent habitual physical activity patterns, as several studies have shown that a higher level of physical activity in general can improve glycemic control.[33] However, the effect of exercise before or after a meal on glucose concentrations 2 hours later seems to differ greatly between individuals. Additionally, in our model there was no interaction effect between exercise and carbohydrate intake, suggesting that the influence of exercise on glucose concentrations is not dependent on prior carbohydrate intake. The American College of Sport recommends exercise for people with type 2 diabetes to lower glucose values, especially in the postprandial period.[34] Our results suggest that for some people the glucose-lowering effects of exercise may not be as large as one might expect. Also, from our model it seems not all individuals with type 2 diabetes may benefit from postprandial exercise specifically; for some individuals, preprandial exercise may be more effective. It should be noted that we only modeled the effect of exercise on glucose concentration 2 hours later. Also, physical activity has multiple health benefits besides contributing to improved glycemic control.[35]

Specifically looking at the effects of moderate-intensity physical activity, which was also recommended during the exercise interventions in our study, there is quite some variation in the effects on glucose levels among studies.[11–13 21 25] While the study design, interventions and outcome measures differ between studies, there seems to be a tendency for non-response and more effect of exercise during the postprandial period as compared with before. Also, beneficial effects are more often found on a composite measure of glucose over time rather than point estimates of glucose, such as the 2-hour glucose concentration. Nonetheless, in our real-world study, an overall positive effect of postprandial or preprandial exercise on the glucose response was not found. This could be explained by interindividual differences in the effects of physical activity on glucose levels, but it may also be that the time-dependent effect of physical activity on glucose is not being captured by the single time point of the 2-hour glucose concentration.

When considering sleep, our study results are in line with literature, as more sleep was associated with a slightly lower glucose during the day. Cross-sectional research in people with type 2 diabetes shows that a shorter average sleep duration per night is associated with a higher

HbA1c.[36] Additionally, interventional research in healthy participants found that a bad night of sleep can increase insulin resistance by 19–25% the next day.[37] In comparison, the effect of sleep in the present study looks small with a 0.01 mmol/L decrease in 2-hour glucose concentrations for every additional hour of sleep. Given that our study did not include a sleep intervention, our data do not include many examples of more extreme sleep conditions such as a 4-hour night or an excessively long night of good sleep. As indicated by the PSQI results, our study population had a poor sleep quality and slept 6.45 hours per night on average, with a small SD of 1.25 hours. The low variability in sleep data might explain the relatively small effect of sleep on glucose levels found in our study, as compared with what is currently known.

People with type 2 diabetes can differ in insulin resistance and insulin production especially between people with or without insulin treatment. Our study population was homogeneous. It consisted of individuals with well-managed type 2 diabetes using only metformin or no diabetes-related medication. The majority of people had an HbA1c below 7% mmol/L. Although this represents the largest group of people with type 2 diabetes, this affects the generalizability of our results. Our study does show the feasibility to generate more personal estimates of how lifestyle might affect glucose values. This approach could in the future be expanded to a more heterogeneous group of people with type 2 diabetes.

The data collection process itself posed potential biases. Particularly biased is the collection of nutritional data, where accurate and consistent collection can be challenging. To mitigate this, we implemented several measures, including a thorough review of the data by experts to identify and rectify large errors, upfront training for participants, and a simplified data entry system for meals delivered during the diet intervention. Despite these efforts, the inherent difficulty in obtaining precise nutritional information remains a limitation. Furthermore, the exercise data were collected using Fitbit devices, which only measured steps and heart rate, and extrapolated the METs from these measurements. This approach lacks differentiation in exercise types and should therefore be interpreted more on the area of moderate-intensity exercise. Nevertheless, moderate-intensity exercise is one of the main preferred methods in the treatment of diabetes.[38]

To summarize, in our linear mixed effects model, exercise in the past 12 hours and sleep duration were associated with a lower glucose concentration 2 hours later, while a higher carbohydrate intake and a higher current glucose level were associated with a higher glucose concentration 2 hours later. The direction of the effects of exercise before and after a meal on glucose control seems individually determined as indicated by the fact that the coefficients for the random effects for exercise in the past 30 and future 30 min were centered around 0, with both positive and negative effects on glucose concentrations 2 hours later. For carbohydrate intake, mainly the magnitude of the effect differed between individuals, with both a positive fixed and mainly positive random effects of carbohydrate intake on glucose concentrations 2 hours later. Knowing the acute effects of lifestyle factors on glucose concentrations for an individual is a prerequisite for precision lifestyle recommendations for improved glycemic control, for example, to avoid high glucose values in people with type 2 diabetes.

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Contributors TS conducted the clinical study, researched data, contributed to discussion, and wrote the first draft of the manuscript. IMdH conducted the clinical study, wrote the first draft of the manuscript, contributed to discussion, and reviewed and edited the manuscript. TK conducted the statistical analyses and contributed to discussion. RJMK conducted the clinical study. HME, AAdG, TK and HP contributed to discussion and reviewed and edited the manuscript. All authors approved the final version of the manuscript. TS is the guarantor.

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Competing interests TS has a paid position at Roche Diagnostics Netherlands that markets tools related to diabetes self-management.

Patient consent for publication Not applicable.

Ethics approval This study involves human participants and was approved by the Ethics Committee of METC Brabant (protocol code P1934, ID: NL70771.028.19) on October 28, 2020. The study was conducted in accordance with the Declaration of Helsinki. Informed consent was obtained from all subjects involved in the study. Participants gave informed consent to participate in the study before taking part.

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Data availability statement Data are available upon reasonable request. The raw anonymized data supporting the conclusions of this article will be made available by the authors on reasonable request.

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