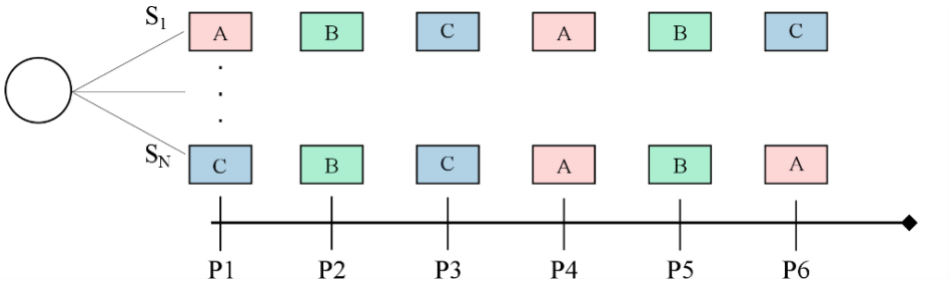
Supplementary Material

1 Study Design and Participant Allocation



Supplemental Figure 1: Crossover study design schematic. Each subject S_i (of n =12) was randomly assigned to a sequence of six meal sessions that took place at six periods (six separate visits) with a 48h interval between them. The meal sequence consists of the three study meals (A, B and C) and a repetition of each meal. The design was uniform within sequences (each subject had all type of meals) but not across periods (each meal did not appear the same number of times within each period).

2 Statistical Analysis

All outcomes were evaluated using linear mixed effect regression models (LMEM) in which outcomes are included as dependent variables while the meal type is included as a fixed effect and subject identifiers as random effects, considering a random intercept. Additionally, to control for the confounding effect of breakfast on the study outcomes, several covariates were evaluated in the LMEM selection process as fixed effects (see section 2.1). Subject demographic and anthropometric characteristics at baseline (age, gender, BMI, waist and hip circumference) were tested in the LMEM as potential covariates. Period effects were considered as fixed effects to account for non-uniformly distributed meals across periods.

2.1 Peak Glucose

In two of the study sessions a distinct meal peak could not be detected due to potential effect of previous meals combined with active insulin on board and therefore, the peak value was set to unknown. The fixed effects that yielded the best model fits (determined by the Akaike information criterion (AIC) values in a forward selection manner) are the following (see equation below): 1) meal type effects ($M_{A,B,C}$), 2) CGM at the start of the meal (CGM_0), to account for different starting CGM values, 3) baseline rate of glucose change (CGM_{rate}), computed as the average rate of change over 15 min prior to the start of the meal using a moving average filter for CGM to minimize the effect of noise artifacts; this factor was included to account for lingering effect of the previous meal on the study meal, 4) CGM at the end of the study session (CGM_{end}), to control for cases where the 5 hours postprandial period was not enough to diminish the effect of the meal and glucose values had not returned to baseline, 5) the bolus amount ($Bolus$), although every subject gave the same amount of insulin for each meal, this factor was included to account for cases of bolus miscalculations (over-under estimation), 6) the daily insulin amount per subject weight (TDD/kg), this factor was considered to account for the background insulin that was given throughout the day, 7) hypoglycemic treatment ($HypoTreat$) as a binary variable was added to account for glucose increase after a treatment in the case of a hypoglycemic event during the observational period, and finally 8) the period effects ($P_{2,..6}$), to account for non-uniformly distributed meals across periods. Demographic or anthropometric characteristics did not affect glucose peak and therefore were omitted from the model.

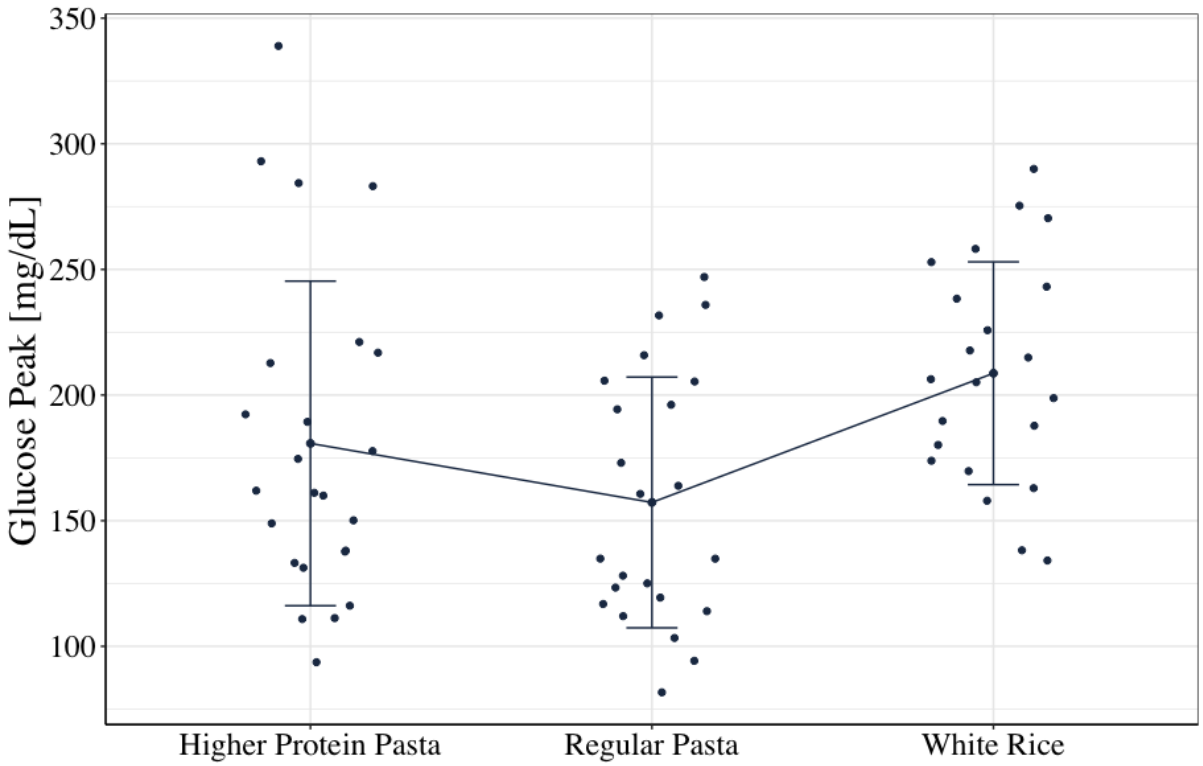
$$Y_{ij} = \beta_1 + \beta_2 M_A + \beta_3 M_B + \beta_4(CGM_0) + \beta_5(CGM_{rate}) + \beta_6(CGM_{end}) + \beta_7(HypoTreat) + \beta_8(Bolus) + \beta_9(TDD/kg) + \beta_{10}(P_2) + .. + \beta_{15}(P_6) + b_{ij} + e$$

Peak glucose differences are presented in Table 1 in the main manuscript. Summary descriptive statistics of key outcomes are listed below in Supplemental Table 1. Individual glucose peaks per subject per meal are plotted in Supplemental Figure 2.

Supplemental Table 1: Summary descriptive statistics of key outcomes (mean ± SD)

	Peak Glucose (CGM) (mg/dL)	**Area Under the Curve (AUC) [5h] (mg/dL x 300min)**	**Time to Peak (min)**
Higher Protein Pasta	180.8 ± 64.6	42,060.1 ± 16,608.2	86.8 ± 33.4
Regular Pasta	157.3 ± 49.9	35,843.6 ± 12,741.1	74.7 ± 30.6
White Rice	208.7 ± 44.3	49,331.2 ± 10,174.9	114.5 ± 33.0

Supplemental Figure 2. Glucose peak (mg/dL) values for each subject and each meal (each meal was given twice to the same subject). Error bars represent the standard deviation of data set.



2.2 Area Under the Curve (AUC)

The LMEM structure to evaluate the effect of the three meals on AUC is the same as the one for the peak glucose. The results of the meal effect on the 5-hour AUC are presented in Table 3 in the main manuscript. The effect of the three meal types on the 0-3h or 3-5h post prandial period, defined as 3 hours from the meal start and between 3 and 5 hours respectively, was also

evaluated (Figure 2 in the main manuscript). The covariates in these two models, although were conceptually identical to the model used for the AUC of the entire postprandial period, were updated to describe the distinct time periods. Specifically, for the 0-3h period, the final CGM was the CGM reading at 3h, the hypoglycemia treatment was 1 (binary variable) only when a treatment to a hypoglycemic event was given between 0-3 hours from the start of the study. Similarly, for the 3-5h period, CGM at start of the meal is the CGM reading at 3h and the rate of change is the average rate of glucose change for 15min prior to 3h.

3 Sub-Analysis

3.1 Within-Subject Variability

Each meal was consumed twice and therefore the day-to-day variation in glucose response can be estimated. The difference of glucose peak, AUC and time to peak between the two repetitions for each meal was obtained by using a LMEM with identical structure as considered previously to control for other factors that may have influenced the effect of the meals. In more detail, each meal is considered separately and for a given outcome (dependent variable), the effect of the meal represents the effect of each meal for repetitions 1 and 2 ($Y_{i,j} = \beta_1 + \beta_2 M_{m,2} + \ldots$ where $m = A, B, C$), whereas the other fixed and random effects are kept the same. The mean difference (95% CI) between repetition 1 and 2 for regular pasta was -5,746.36 mg/dlxmin (95% CI -6,953.5, -2,337.4; p=0.04). Concerning glucose peak and time to peak, the mean difference between the repetitions 1 and 2 for each meal was not statistically significant. For the higher protein pasta and white rice, the mean difference between all considered metrics between repetitions 1 and 2 was not statistically significant.

3.2 Postprandial Hypoglycemia

The percent time glucose was spent in the glycemic range below 70 mg/dL was calculated and the outcome metric was transformed to a binary variable representing the event of hypoglycemia (1) or not (0). A generalized LMEM using a logit link function was fitted using the same fixed and random effects as described previously. Additionally, baseline hemoglobin A1C was also added as a fixed effect, to account for potential suboptimal insulin management. The odds of hypoglycemia for regular pasta was 14 times (95% CI 1.0, 184.0; p=0.04) more likely than for the higher protein pasta. Compared to white rice, the event rate of hypoglycemia for regular pasta was 1,417 times more likely to occur (95% CI 11.0, 1.77×10^5; p=0.003). For the higher protein pasta, the event of hypoglycemia was 101 times more likely to occur compared to white rice (95% CI 1.2, 405.0; p=0.01).