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A Pilot Study of the Effect of Evening Almond Butter Consumption on Overnight and Fasting Interstitial Glucose

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Abstract: Approximately 40% of patients with type 2 diabetes (T2D) experience an early-morning rise in fasting glucose that is not effectively treated by available oral hypoglycemic agents. This study aimed to determine the acute effect of consuming almond butter as an evening snack on fasting and overnight interstitial glucose, compared to a no-snack control, in people with T2D. Adults with T2D, not taking insulin, were recruited to participate in this two-week randomized, controlled, crossover pilot study. Participants received 2 tbsp of natural almond butter as an evening snack, or a no-snack control, for one week each. Glucose was measured by continuous glucose monitor (CGM). Analyses were performed using linear mixed effect modeling in R. Ten adults (60% female; age: 57 ± 5.6 years) completed the study. The intervention did not significantly influence fasting glucose [4–6 a.m.; $\beta = 5.5$, 95% CI = $[-0.9, 12.0]$, $p = 0.091$; Marginal R² = 0.001, Conditional R² = 0.954] or overnight glucose (12–3 a.m.; $\beta = 5.5$, 95% CI = $[-0.8, 11.8]$, $p = 0.089$; Marginal R² = 0.001, Conditional R² = 0.958). Significant variability in continuously measured glucose was observed. These findings will inform the design of a larger investigation.

Keywords: fasting glucose; almonds; almond butter; continuous glucose monitoring; interstitial glucose; type 2 diabetes



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1. Introduction

There are approximately 37 million people with diabetes in the United States and 96 million people with prediabetes [1]. Worldwide, estimates suggest that 1 in 10 individuals will develop type 2 diabetes (T2D) by 2035, with the cost of diabetes care and comorbid conditions being almost twice that for those without diabetes [2]. Only about half of US adults with diabetes meet evidence-based standards for glycemic control [3]. Poor control increases the risk of cardiovascular disease [4], but these risks can be moderated through optimal diabetes control including hemoglobin A1C of <7% (53 mmol/mol) for nonpregnant adults [5].

Individuals with elevated fasting glucose may experience increased hepatic glucose production, decreased glucose clearance, impaired insulin production and secretion, or a combination of these [6]. The Dawn Phenomenon is the rise in fasting glucose that occurs early in the morning and is not effectively treated by currently available oral hypoglycemic agents [7]. In T2D, it is hypothesized that the Dawn Phenomenon is caused by excessive hepatic production of glucose “at dawn” in the presence of diminished insulin release to counteract the corresponding rise in blood glucose [8,9]. This phenomenon affects up to 40% of people with T2D without an obvious relation to glycemic control, or treatment modality [7]. A rise in fasting blood glucose levels may result in daylong hyperglycemia and may be an independent risk factor for T2D in those with normal glucose tolerance [10]. The need for

improved glycemic control strategies is evident from the increasing prevalence of T2D and the frequency of poor glycemic control. Moreover, in the clinical setting, patient adherence to diabetes pharmacotherapy is low and many therapeutic options have the potential for side effects [11]. As such, an evidence-based, affordable nutritional intervention that improves glycemic control non-pharmacologically would increase the number of treatment options available to patients with diabetes and their healthcare providers.

Nuts have cardioprotective and glucoregulatory properties. A systematic review and meta-analysis of observational studies found an inverse relationship between nut intake and heart disease and all-cause mortality, but not T2D [12]. A systematic review and meta-analysis of intervention studies found no effect of nuts on fasting glucose, but favorable effects on HOMA-IR and fasting insulin [13]. Almonds contain monounsaturated fat (MUFA), plant protein, fiber, B-vitamins, vitamin E, magnesium and arginine, all of which may have a favorable impact on blood glucose control [12]. Considering the effects of almonds and almond butter on other markers of diabetes control including post-prandial blood glucose and circulating insulin levels, there is biologic plausibility that consumption of almonds as an evening snack may improve fasting glucose levels [13]. However, previous studies have included healthy populations; therefore, findings cannot be generalized to people with impaired glycemic regulation, e.g., people with T2D. Additionally, many of the studies done to date have not included nutrition counseling on timing of consumption, serving sizes, and dietary incorporation. The effect of consuming almonds as an evening snack on fasting glucose levels has not been tested. Thus, we aimed to determine the acute effect of consuming almond butter as an evening snack on fasting interstitial glucose levels and overnight glucose changes, compared with usual intake, in people with T2D. Secondary endpoints included post-prandial interstitial glucose trends (2–3 h after meals, variability, and other time series metrics), as recorded by a continuous glucose monitoring system.

2. Materials and Methods

2.1. Study Design

A randomized, 2-period crossover, pilot study was conducted. In random order, participants with T2D were assigned to: (1) consume 2 tablespoons (tbsp) of natural almond butter as an evening snack (after dinner, but before bedtime) and not to consume any other caloric foods or beverage in the evening; (2) no consumption of caloric foods or beverages after dinner (no snack control). Participants experienced each condition for 1 week and then crossed over to the other condition without a break. No washout period was necessary as no carryover effects were expected from this intervention. Randomization was completed using Randomization.com. All participants provided written informed consent. This study received approval from the Pennsylvania State University Institutional Review Board (STUDY00008991) and is registered at [ClinicalTrials.gov](https://clinicaltrials.gov) (ClinicalTrials.gov Identifier: NCT03826472). Participants were compensated \$100 for successful completion of the study. They were also entered into a gift card drawing (two \$25 gift cards).

2.2. Participants

Participants were recruited from the State College, PA area from May 2019 to January 2020. Advertisements were placed in campus buildings and facilities, on webpages (<http://clinicaltrials.gov>, <https://studyfinder.psu.edu>, Facebook) and flyers were provided to a local family medicine practice. We recruited adults 18 to 75 years of age with physician-diagnosed T2D, not on insulin therapy or other medication that could cause hypoglycemia (e.g., sulfonylureas, thiazolidinediones). Eligible individuals were either not taking oral antihyperglycemic agents, oral antihypertensive agents, or statins, or had been on a stable dose of any of these for at least 6 months. In addition, current home self-monitoring of blood glucose levels via glucometer or willingness to learn to perform at-home fingerstick glucose measurements and adhere to the study protocol were inclusion criteria. We excluded individuals with type 1 diabetes, kidney disease, liver disease, cancer or inflammatory conditions (e.g., GI disorders, rheumatoid arthritis), women who were

pregnant, breastfeeding, or had been within the previous 6 months, individuals who smoke or use tobacco products, reported an allergy to any tree nut or medical adhesive.

2.3. Study Food

Natural almond butter was purchased from Sam's Club (Member's Mark Creamy Almond Butter; ingredients: dry roasted almonds, salt). The almond butter was mixed in a large mixer (to emulsify following natural separation of oil from almond butter) and pre-portioned into 2 tbsp (32 g) servings by the staff at the Metabolic Diet Study Center on the Penn State University campus. Participants were instructed to consume one serving per night during the almond butter week after dinner and before bed. In addition, instructions were given not to consume anything else besides water unless it was medically necessary (i.e., to prevent hypoglycemia). During the control week, participants were instructed not to consume anything but water after dinner. They were instructed to keep the rest of their diet and lifestyle the same throughout the study. Compliance was assessed through collection of empty almond butter containers and review of food data entered in study smartphones.

2.4. Continuous Glucose Monitoring

Dexcom G4 PLATINUM continuous glucose monitoring systems (CGMS) were donated to the Penn State Cardiometabolic Lab by Dexcom (San Diego, CA, USA). Briefly, a fine needle or sensor is inserted under the skin on the abdominal region and a transmitter is attached overtop to send data to a receiver that the participant carries. The CGMS samples interstitial glucose and transmits values every five minutes. This allows for analysis of glucose at specific time points, as well as analysis of glucose trends over time. Outcomes for this study were measured using the CGMS- interstitial fasting glucose and overnight glucose trends.

Sensors are approved for seven days of wear and therefore each participant required a minimum of two sensors, one for each week of the study. Receiver shields were placed on each receiver and all equipment was sanitized between uses. The CGMS were utilized in accordance with manufacturer's instructions. CGMS were set to the blinded mode so that participants could not see their glucose values in real time.

2.5. Study Visits

Study staff contacted individuals who responded to ads for a phone screening. Once individuals qualified based on the phone screening and were cleared by a clinician (Nurse Practitioner or Physician) at the Clinical Research Center (Penn State University) they were enrolled in the study. The study included three visits to the Clinical Research Center (Figure 1). At visit 1, participants were given instructions on insertion of the Dexcom sensor and inserted the sensor themselves with guidance from study staff. Participants were taught to calibrate the Dexcom G4 device and instructed to calibrate it twice per day with a fingerstick glucose measure, according to manufacturer instructions. If a participant had not been self-monitoring their blood glucose at home, they were provided with a glucometer (Bayer Contour), test strips and lancets and taught to test their blood glucose. Participants were also taught to use the study smartphone and practiced entering their dietary intake data. At visit 2, the first sensor was removed, and the participant inserted a new sensor.

2.6. Data Preparation

All CGM data were uploaded into Dexcom's CLARITY (dexcom.com/clarity) and Studio software. Data were exported for analyses at the level of 5 min samples. Subsequent data preparation steps occurred in R, version 3.6.2 [14]. For each participant, day in study and week in study were calculated against the baseline appointment where participants received the Dexcom unit. For each person-day in the study, finger stick compliance was calculated (suggested 2× per day), number of CGM values (up to 288 per day), number of reported meals (from the smartphone survey), person-mean glucose at three

time windows (whole day, 4–6 a.m.—i.e., fasting, and 12–3 a.m.—i.e., overnight glucose). These windows were selected by reviewing participant data. The fasting window was calculated by reviewing the first calibration of the day and by reviewing food entry data to determine first meal of the day and reverting back approximately two hours. The overnight window was determined by reviewing the last smart-phone entry and last calibration of the evening. For each of these time windows, total area under the curve for glucose (at 15 min increments), was computed, using R package MESS, function, auc [15]. These and other metrics (e.g., average wake time, number of times sampled that they responded having completed a meal) were also computed at the between-person level.

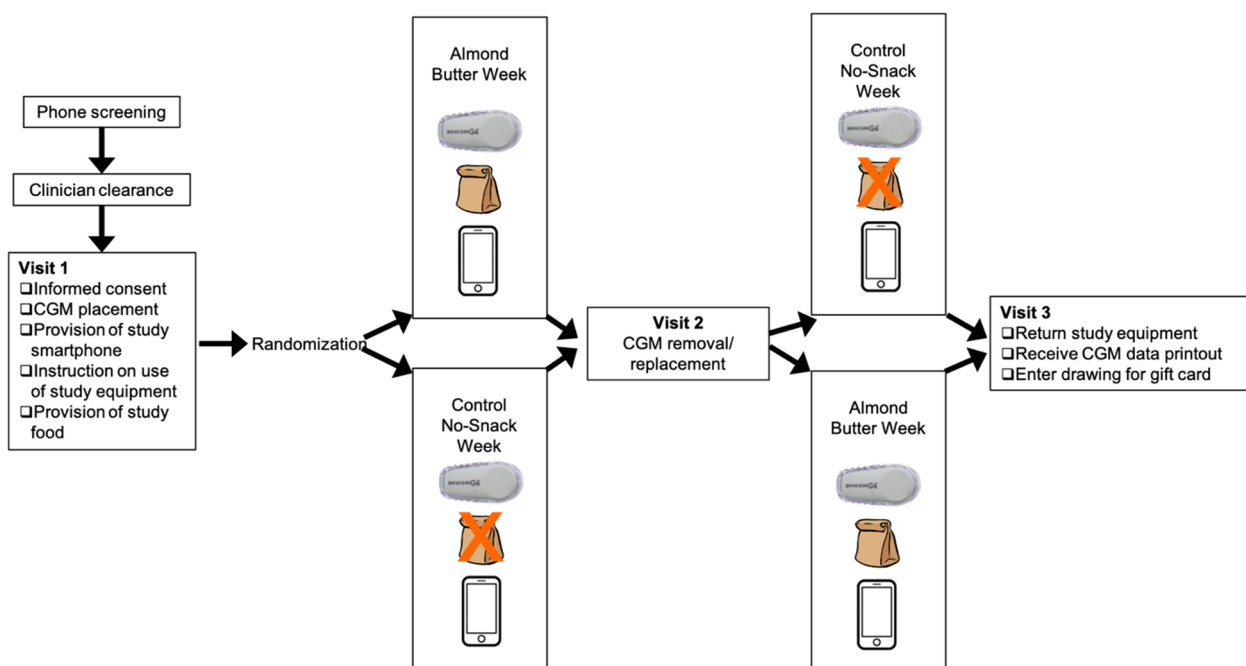


Figure 1. Study Design; Each period was 1 week long with no breaks between periods.

2.7. Statistical Analysis

Sample size calculations were not performed due to the pilot nature of the study and the lack of prior comparable data to use for power calculations. The sample size reflects the resources available. Only individuals that had data for both periods were included in the analyses. Linear mixed effect models were applied to the CGM data aggregated at the level of day (for each person and day in study), and two time windows: fasting glucose (4–6 a.m.) and overnight glucose (12–3 a.m.), using the lmer package in R (version 3.6.3) [16]. Linear mixed effects models were used to account for missing data (from the CGM device), and to better capture participant variability in glucose. For each aggregated outcome, three models were run, each building on the previous. Model one included: condition as a fixed effect, allowing participants their own random intercept. Model two included the additional predictor of week in study (to capture a potential observer effect; interstitial glucose improving with each day in the study). Model three included additional covariates of age, and time since diabetes diagnosis. Statistical significance was set at $p < 0.05$.

3. Results

Ten individuals took part in this study (Figure 2). The baseline characteristics of the randomized participants are shown in Table 1. Seven (70%) were taking oral antihyperglycemic medications; five (50%) participants were taking metformin, one participant was taking metformin plus another oral antihyperglycemic medication, two participants were taking other oral antihyperglycemics without metformin, and three participants were taking no medications for diabetes control. Four participants had not tested their glucose

by fingerstick previously and were taught to use a glucometer and perform a fingerstick. All participants completed the study; one participant was not included in data analysis due to incomplete data collection. Compliance with the study intervention food was 100%.

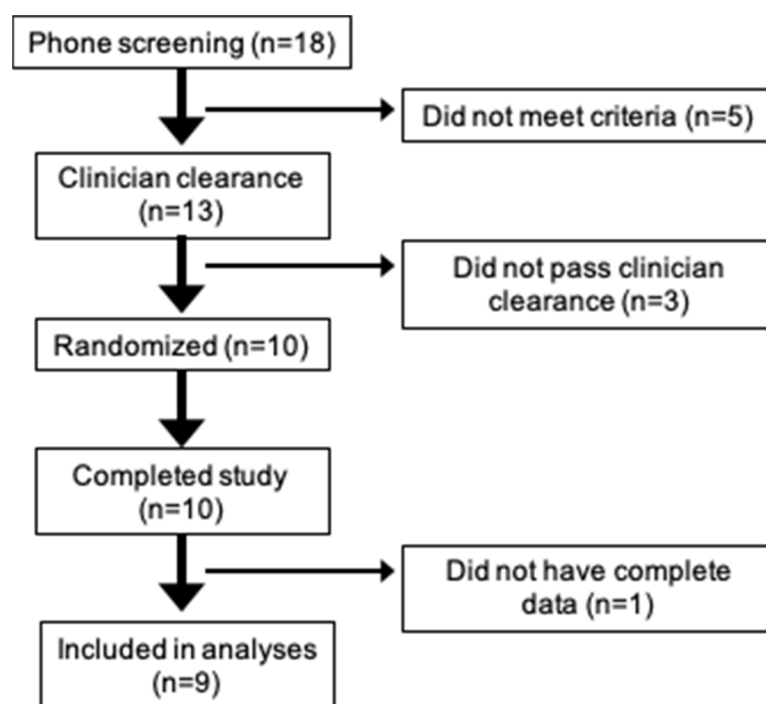


Figure 2. Consort Diagram.

Table 1. Participant characteristics at baseline.

	Mean	Range
Age	57	42–73 years
Gender	6 (60%) female	
Duration of diabetes	5.6 years	3–15 years
Oral Antihyperglycemic Medications		
Yes	7 (70%)	
No	3 (30%)	
Home SMBG prior to study start	6 (60%)	

The mean overnight and fasting interstitial glucose at baseline and end of study by condition are presented in Table 2. The mean average glucose calculated by the Dexcom CLARITY software was 157.7 mg/dL with a range of 96.6–325.2 mg/dL (Table 3). The mean number of CGM samples taken over the two-week study period was 3445. The mean area under the curve for fasting glucose (4–6 a.m.) of the study was 299 mg/dL \times 120 min, with a range from 192.9–623.5 mg/dL \times 120 min and the AUC during the overnight window (midnight–3 a.m.) was 444.6 mg/dL \times 180 min and ranged from 263.5–965.2 mg/dL \times 120 min. The overall mean glucose by condition is detailed in Figure 3. The overall mean fasting glucose for each participant by study condition, overall mean overnight glucose for each participant and study condition and the mean overall glucose for each participant and study condition are displayed in Figure 4.

Table 2. Mean overnight and fasting interstitial glucose at baseline and end of study.

Condition	Overnight Interstitial Glucose (12–3 a.m.)		Fasting Interstitial Glucose (4–6 a.m.)	
	Baseline Mean (SD)	Endpoint Mean (SD)	Baseline Mean (SD)	Endpoint Mean (SD)
Control	108 (32.1) mg/dL 6.0 (1.8) mmol/L	120 (29.1) mg/dL 6.6 (1.6) mmol/L	107 (23.1) mg/dL 6.0 (1.3) mmol/L	128 (19.9) mg/dL 7.1 (1.1) mmol/L
Almond Butter	197 (112.6) mg/dL 11.0 (6.2) mmol/L	186 (107.2) mg/dL 10.3 (5.9) mmol/L	193 (118.9) mg/dL 10.7 (6.6) mmol/L	182 (98.1) mg/dL 10.1 (5.4) mmol/L

Table 3. Summary descriptive statistics of CGM data.

Metric	Overall		Fasting (4–6 a.m.)		Overnight (12–3 a.m.)		Control Week		Almond Butter Week	
	Mean	Range	Mean	Range	Mean	Range	Mean	Range	Mean	Range
Mean glucose, mg/dL (mmol/L)	158 (8.8)	97–325 (5.4–18.0)	150 (8.3)	97–313 (5.4–17.4)	149 (8.2)	88–324 (4.9–18.0)	156 (8.66)	93–318 (5.15–17.65)	160 (8.90)	101–331 (5.60–18.39)
Coefficient of Variation (CV) mg/dL (mmol/L)	20 (1.09)	9–27 (0.49–1.48)	3 (0.18)	0–19 (0–1.07)	3 (0.17)	0–25 (0–1.38)	18 (0.98)	10–24 (0.53–1.33)	20 (1.10)	8–30 (0.45–1.66)
Standard Deviation (SD) mg/dL (mmol/L)	28 (1.57)	14–39 (0.80–2.17)	5 (0.25)	0–48 (0–2.67)	4 (0.22)	0–38 (0–2.13)	26 (1.44)	11–44 (0.62–2.44)	28 (1.58)	16–40 (0.89–2.23)
Time in Range (TIR) *	73.2%	0–98.71%	77.6%	0–100%	77.2%	0–100%	72.74%	0–98.9%	72.49%	0–99.94%
Average Number of CGM samples over study period	3445	1826–3926	-	-	-	-	1813	1635–2008	1813	1485–2074
Total AUC	-	-	299 mg/dL × 120 min (16.6 mmol/L × 120 min)	192.9–623.5 mg/dL × 120 min (10.7–34.6 mmol/L × 120 min)	444.6 mg/dL × 180 min (24.7 mmol/L × 180 min)	263.5–965.2 mg/dL × 180 min (14.6–53.6 mmol/L × 180 min)				

* Time in Range (TIR): percentage of samples within the target range of 70–180 mg/dL (3.8–10.0 mmol/L).

3.1. Primary Endpoint: Fasting Glucose (4–6 a.m.)

Evaluating model one, the Intervention condition did not significantly affect fasting glucose (4–6 a.m.; $\beta = 5.5$, 95% CI = [−0.9, 12.0], $p = 0.091$; Marginal R² = 0.001, Conditional R² = 0.954). Evaluating model two, neither Intervention condition nor week in the study influenced fasting glucose (Intervention condition: $\beta = 5.1$, 95% CI = [−1.3, 11.6], $p = 0.119$; week in study: $\beta = -3.8$, 95% CI = [−10.2, 2.7], $p = 0.254$; Marginal R² = 0.002, Conditional R² = 0.954). Model three showed no significant predictors of fasting glucose (Intervention condition: $\beta = 5.1$, 95% CI = [−1.3, 11.6], $p = 0.119$; week in study: $\beta = -3.8$, 95% CI = [−10.2, 2.7], $p = 0.254$; age: $\beta = -1.8$, 95% CI = [−7.7, 4.1], $p = 0.552$; time since diagnosis of diabetes: $\beta = 4.8$, 95% CI = [−6.2, 15.8], $p = 0.390$; Marginal R² = 0.093, Conditional R² = 0.964). See Table S1 for more details.

3.2. Secondary Endpoint: Overnight Glucose (12–3 a.m.)

Evaluating model one, the Intervention condition did not significantly influence overnight glucose (12–3 a.m.; $\beta = 5.5$, 95% CI = [−0.8, 11.8], $p = 0.089$; Marginal R² = 0.001, Conditional R² = 0.958). Evaluating model two, neither Intervention condition nor week in the study influenced overnight glucose (Intervention condition: $\beta = 5.0$, 95% CI = [−1.35, 11.28], $p = 0.123$; week in study: $\beta = -4.6$, 95% CI = [−10.9, 1.7], $p = 0.152$; Marginal R² = 0.002, Conditional R² = 0.958). Evaluating model three, there were no significant predictors of overnight glucose (Intervention condition: $\beta = 5.0$, 95% CI = [−1.4, 11.3], $p = 0.123$; week in study:

$\beta = -4.6$, 95% CI = $[-10.9, 1.7]$, $p = 0.153$; age: $\beta = -1.5$, 95% CI = $[-7.7, 4.6]$, $p = 0.630$; time since diagnosis of diabetes: $\beta = 4.6$, 95% CI = $[-6.8, 16.00]$, $p = 0.428$. Marginal R2 = 0.076, Conditional R2 = 0.967). See Table S2 for more details.

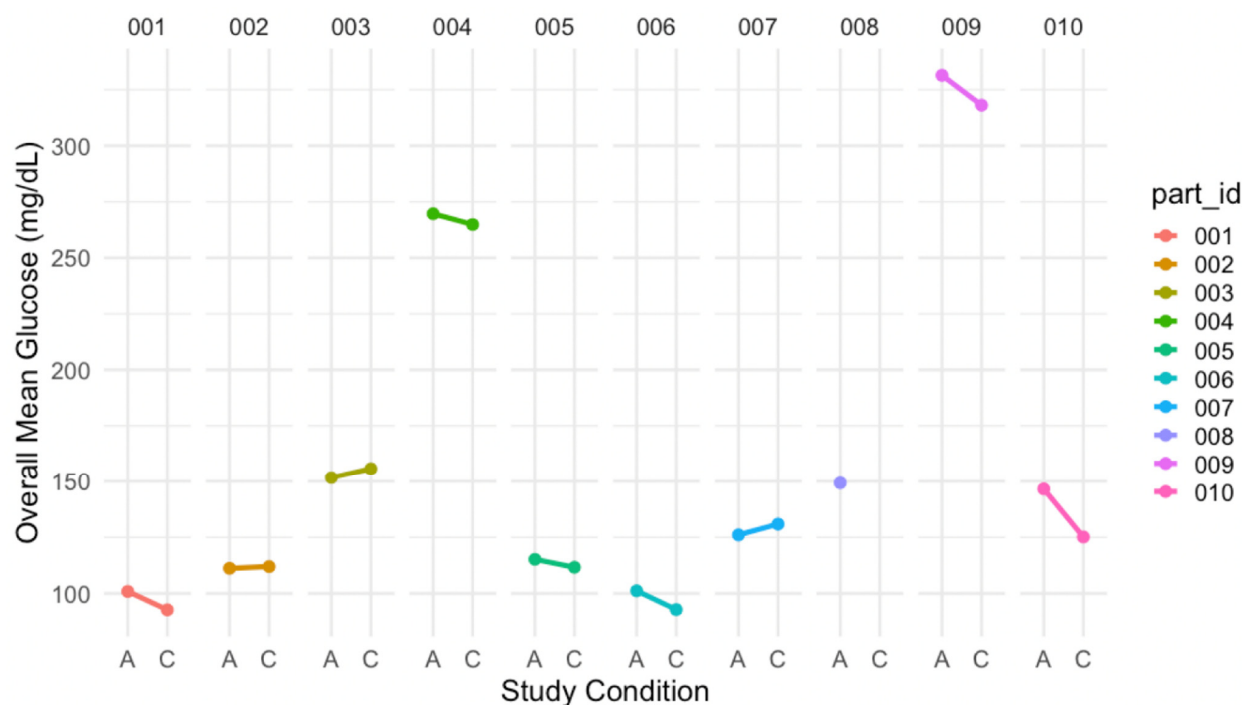


Figure 3. Overall mean glucose (mg/dL) across study conditions, for each participant. Note intercept differences amongst participants.

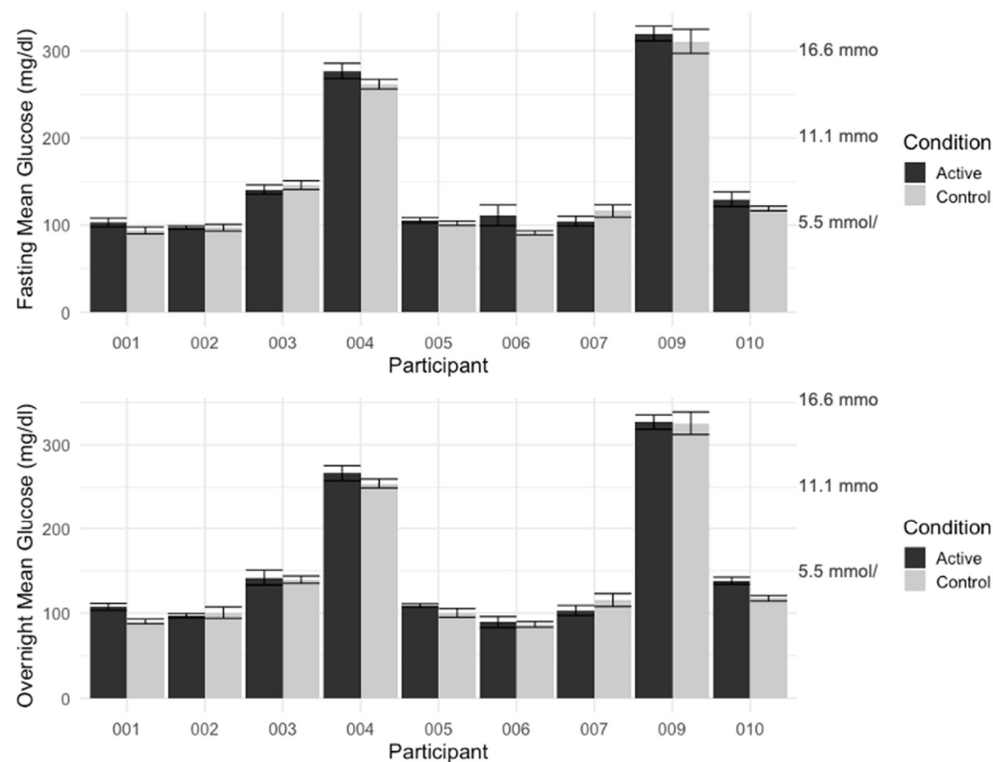


Figure 4. Mean fasting and overnight glucose. (Top) Mean fasting glucose for each participant and study condition. (Bottom) Mean overnight glucose for each participant and study condition.

4. Discussion

In this randomized, controlled crossover pilot study, we found no difference in fasting interstitial glucose between the intervention condition, 2 tbsp of natural almond butter evening snack, and the control condition, no evening snack, in adults with T2D not using insulin therapy. The almond butter was well-tolerated by participants and there were no reports of any adverse effects. Significant between-individual variation was observed that was not attributable to the intervention, although with the sample size and pilot nature of the study we were unable to identify the sources of variation. These pilot findings will inform a larger trial that is adequately designed to understand determinants of glucose variance and the impact of dietary intervention on fasting glucose.

Significant between-person variation in glycemic control and response to glucose-lowering lifestyle interventions is well-documented in diabetes management [17]. In the current study, across both the primary and secondary endpoints, participant random intercepts accounted for most of the variance, thus, indicating that data of this type may be suited to person-specific, N-of-1 modeling approaches. For example, the marginal R² value for the primary endpoint of fasting interstitial glucose, was 0.001, while the conditional R² was 0.954; similarly, for the secondary endpoint, the marginal R² was 0.001 and conditional R² was 0.958. The ICCs for models one through three, across both endpoints, ranged from 0.95–0.96, indicating a high degree of similarity from values from the same group (i.e., the participant). To further emphasize the need for person-specific modeling, see Figure S1, showing within-person variation in glucose as a function of study week.

The timing of the snack intervention was an important consideration in the planning of this study. A study in 15 adults with T2D found that administration of a low carbohydrate snack at bedtime, an egg, improved fasting glucose and insulin sensitivity compared to a high carbohydrate snack of yogurt. When compared to no snack at dinner, there was no difference. This was a 4-day intervention and participants also wore continuous glucose monitors [18]. In a study involving adults with T2D, a pre-bedtime snack (Extend bar) containing 5 g of uncooked cornstarch improved fasting glucose compared to a control bar without uncooked cornstarch [19]. Uncooked cornstarch is a slow digesting, complex carbohydrate and the addition of it to this snack prevented blood glucose excursions over the proceeding 6 h. This overnight regulation of blood glucose may help prevent or attenuate morning fasting hyperglycemia that is common in individuals with T2D. In contrast, a study in a group of 68 pregnant females with gestational diabetes found that a high and a low carbohydrate evening snack led to increased fasting glucose over the five-day intervention period [20]. Glucose was measured by at-home finger-stick only. These studies reflect the evolving nature of our knowledge of the impact of dietary choices on fasting glucose.

Fasting blood glucose remains an important treatment target in diabetes care in part due to evidence that fasting blood glucose variability over the long term is an independent predictor of mortality in patients with T2D [21]. Elevated fasting glucose contributes to increased Hemoglobin A1c to a greater extent in patients with poorly controlled diabetes (HbA1c > 9%; IFCC HbA1c: 75 mmol/mol) than better controlled diabetes [22] (HbA1c < 7% (53 mmol/mol) for nonpregnant adults [5]). Identifying new patient-centered and cost-effective approaches to control fasting glucose, and therefore improve HbA1c levels, will support the goals of patients, healthcare providers and health systems alike. Interventions that target small lifestyle changes, such as a change in evening snack, may be well-suited to patients already on pharmacotherapy for diabetes, and for those with prediabetes or early stages of T2D in which medications may not yet be indicated or desired by the patient.

There is a growing body of evidence showing that nut consumption improves longer term glycemic control and risk factors for cardiovascular disease [13,23]. A meta-analysis of 12 randomized controlled trials, including 450 participants, showed that tree nut consumption reduced fasting blood glucose in individuals with T2D by 2.5 mg/dL (0.15 mmol/L) ($p = 0.03$) in approximately 8 weeks. The addition of almonds to a meal helps to reduce the

glycemic index of the meal and may help to reduce glycemic response [24]. In a 12-week randomized crossover trial in adults with T2D, adults who consumed 20% of calories from almonds saw a reduction in fasting insulin, fasting glucose, and homeostasis model assessment of insulin resistance (HOMA-IR) compared to the control diet [25]. In a four-week randomized, parallel-arm study of timing of almond intake, participants with increased risk for T2D consumed 43 g of almonds at different times of day. Those consuming almonds reported reduced hunger and desire to eat and saw reductions in postprandial glucose levels; this effect was greatest in those consuming almonds as a snack [26]. The nutrient profile of almonds, including MUFA and fiber, which delay gastric emptying and stabilize overnight blood glucose levels, and arginine which may improve insulin sensitivity through increased insulin secretion and glucose uptake, may be drivers of these positive effects on glycemic control [12,27,28].

In the clinical setting, poor glycemic control is common, with 60% of patients with T2D demonstrating poor knowledge of dietary intake as a cornerstone for diabetes self-care [29]. Diabetes education is effective, but underutilized. Complications from poorly controlled diabetes create an immense burden on health care delivery systems. The addition of a simple dietary intervention that effectively improves glycemic control without additional medication has the potential to improve long-term quality of life for persons with diabetes by preventing or slowing complications. Such an approach may help patients with diabetes more effectively reach HbA1C goals for glycemic control, thereby reducing eventual microvascular complications, such as diabetic retinopathy and cardiovascular events. In addition, providing evidence-based data to healthcare providers who treat T2D would be useful for offering practical nutrition counseling that can moderate outcomes.

In some individuals the Dawn Phenomenon is thought to be responsible for elevated fasting glucose; however, there is no standard methodology for assessing whether an individual is experiencing the Dawn Phenomenon. Therefore, in our study we did not screen participants for the Dawn Phenomenon. Utilizing a similar method to Monnier et al. [7], we calculated how many days participants experienced a >20 mg/dL difference in interstitial glucose between 4 and 6 a.m. as an indicator of the Dawn Phenomenon. In total, seven of the ten participants experienced at least one occasion and three participants experienced more than one day where the difference in interstitial glucose was suggestive of the Dawn Phenomenon; there was no relationship to condition or outcome (data not shown). Therefore, it is possible that we did not see the hypothesized effect because the participants in our study were not regularly experiencing the Dawn Phenomenon. In future studies, response to dietary intervention may be examined by presence/absence of Dawn Phenomenon.

Given the short duration and serving size (1 portion of almond butter), we do not expect that any carryover effects were present in this study. Randomization of the condition order helped to eliminate this potential study confounder. Nuts and nut butters are calorically dense and therefore portion control is important for weight management, especially in a population with T2D where weight can impact glycemic control. A recent systematic review found no association between dose of nuts and glycemic control where the dose ranged from 20 g/d to 113 g/d [13] and therefore we cannot conclude that the standard serving size of the almond butter was inadequate to generate effects. The limitations of this study were the small sample size and the short duration. Data on weight and BMI were not collected; however, given the small sample, short duration and crossover design, we do not expect this impacted the outcomes. Collection of further demographic and health data would allow for subgroup analyses to compare responders and non-responders, so this is recommended for future studies. We also did not collect data on nut intake prior to the start of the study or baseline fasting or postprandial glucose measurements. Participants were instructed to consume their snack after dinner and before bed, but no time was specified. This could have had an impact on the outcome of the study if the timing of the snack varied significantly. Dietary data were collected via study smartphone for compliance purposes and was not adequate to measure diet quality or other dietary indices. This was a pilot study and allowed us to gather information and test methods, but the findings are not

generalizable to the larger population at this time. Additionally, while the CGM displays were blinded, participants were able to see the glucose values when they performed finger sticks. This was unavoidable due to the need for calibration. Participants who had not been previously testing their glucose via fingerstick were able to see their glucose regularly and some made dietary changes throughout the weeks as a result, even though they were asked to keep their diet and activity stable throughout the two-week study. This may have affected the results. Future studies should ensure that participants can remain blinded to their glucose values, particularly if they had not been routinely testing their glucose prior to enrollment. Future studies would also benefit from collecting anthropometric information and more detailed dietary records.

According to NHANES 2009–2010, approximately 38% of US adults consumed nuts on a given day [30]. However, 22% of those men and about 28% of those women consumed less than the recommended 1.5 oz, possibly due to concern over the calorie and fat content of nuts. Increasing awareness of the nutritional benefits of almonds may result in higher levels of almond intake and improved nutrient profile of the diet due to the contribution of almonds to the diet compared to the average snack. While nighttime snacking has a negative health connotation due to the quantity and poor quality of foods generally eaten as snacks, an evening snack can be a healthy way to improve metabolic health if small and calorie-controlled [31].

In conclusion, in this randomized, controlled, 1-week, crossover pilot study we observed no difference in fasting or overnight interstitial glucose with intake of 2 tbsp of natural almond butter as an evening snack compared to no evening snack in adults with T2D not using insulin therapy. This pilot research provides data and insights that may assist in the planning of future studies that are adequately powered and designed to investigate the effect of nutrition interventions on glycemic control with requisite consideration of inter-individual variability and assessment of variables that may explain variability. This knowledge may assist investigators working in the area of precision nutrition.

Supplementary Materials: The following supporting information can be downloaded at: <https://www.mdpi.com/article/10.3390/diabetology3040038/s1>, Table S1: Results for overnight glucose (12–3 a.m.) outcome across three models. Table S2: Results for overnight glucose (12–3 a.m.) outcome across three models, Figure S1. Individual differences in within-person variation.

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Data Availability Statement: The datasets generated during and analysed during the current study are available from the corresponding author on reasonable request.

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