Randomized Crossover Trial

Lifestyle Habits as Potential Predictors of Impaired Blood Glucose Regulation in Patients with Chronic Low Back Pain vs. Healthy Controls: A Secondary Analysis of a Randomized Crossover Trial

M. Elena Gonzalez-Alvarez, MsC[1-4], Ömer Elma, PhD[5-7], Perseverence Savieri, MsC[8], Sevilay Tumkaya Yilmaz, MsC[5], Peter Clarys, PhD[6], Tom Deliens, PhD[6,9], Jorge Hugo Villafañe, PhD[10], Jo Nijs, PhD[7,11,12], Josué Fernández-Carnero, PhD[2,3], and Anneleen Malfliet, PhD[7,11,12]

From: See page 535 for author affiliations.

Address Correspondence: Anneleen Malfliet, PhD Pain in Motion Research Group (PAIN), Department of Physiotherapy, Human Physiology and Anatomy, Faculty of Physical Education and Physiotherapy Vrije Universiteit Brussel, Brussels, Belgium E-mail: anneleen.malfliet@vub.be

Disclaimer: M.E. Gonzalez-Alvarez and O. Elma are shared first authors. There was no external funding in the preparation of this article.

Conflict of interest: Jo Nijs is the holder of a chair titled Exercise Immunology and Chronic Fatigue in Health and Disease funded by the Berekuyl Academy/European College for Lymphatic Therapy of the Netherlands. Anneleen Malfliet has received a personal grant from the Research Foundation—Flanders (FWO) of Brussels, Belgium. Ömer Elma and Sevilay Tumkaya Yilmaz are funded by the Republic of Turkey's Ministry of National Education as scholarship students for their PhD research program.

Article received: 11-27-2024
Revised article received: 04-28-2025
Accepted for publication: 06-26-2025

Free full article: www.painphysicianjournal.com

Background: Chronic low back pain (CLBP) affects over 20% of adults worldwide. Despite the socioeconomic burden caused by this condition, there is no gold standard treatment for CLBP, and its etiology remains nonspecific in 85% of cases. Available evidence indicates that CLBP patients have higher postprandial glycemic responses to beverages that rank high on the glycemic index and that this finding correlates with pain severity. Therefore, understanding modifiable factors that predict blood glucose regulation in CLBP patients could reveal important information for the management of the condition.

Objectives: This study aimed to (1) examine the relationship between predictor variables and the overall glycemic response, measured by the incremental area under the curve (IAUC), and (2) assess the temporal changes in patients' blood glucose levels immediately after sucrose intake. This dual approach enables a nuanced understanding of both the cumulative and immediate impacts of sucrose intake on glycemic control, facilitating insights into personalized management strategies for mitigating glycemic variability.

Study Design: A secondary analysis of a case-control randomized controlled crossover trial to identify predictive factors for impaired blood glucose regulation.

Setting: Vrije Universiteit Brussel, Belgium.

Methods: Individuals with chronic low back pain (CLBP) were randomized to consume either a sucrose or isomaltulose beverage. Body composition, dietary intake, physical activity levels, psychological factors, and blood glucose levels were measured. Multiple linear regression was used to examine the relationship between baseline variables and postprandial glucose response following intake of the high–glycemic index beverages, and a linear mixed model (LMM) was applied to assess the relationship between sucrose intake and identified potential predictors.

Results: Our findings revealed that higher weight ($P < 0.001$; t = -4.06), higher age ($P = 0.003$; t = 3.06), higher inflammatory dietary properties ($P = 0.025$; t = 2.28), worse mental health ($P = 0.021$; t = 2.34), and lower diet quality ($P = 0.002$; t = 3.22) were associated with a significant predictive value for altered postprandial sucrose responses.

Limitations: This study is a secondary analysis of a crossover case-control trial, so causal interpretations should be made cautiously. Additionally, postprandial glucose was measured using a self-monitoring finger-prick device, which lacked real-time data, and the findings were specific to women and may not apply to men.

Conclusion: These results confirm the potential relevance of targeting lifestyle factors in people with CLBP.

Key words: Low back pain, body composition, age, diet, inflammation, mental health, healthy controls, secondary analysis

Pain Physician 2025: 28:527-537

Low back pain is recognized as the leading cause of disability worldwide (1,2). The condition is characterized by high prevalence rates and many progressing into chronicity (i.e., chronic low back pain [CLBP], defined as pain persisting for more than 3 months) (3,4). Despite the high socioeconomic impact of CLBP, there is to date no gold standard treatment for the condition, with current strategies showing only moderate treatment effects (5). Moreover, the etiology in over 85% of cases is classified as nonspecific, highlighting the complexity of this condition (6).

Given the limited efficacy of existing treatments for CLBP, uncovering the mechanisms of the condition is needed to guide the development of novel therapeutic strategies for it. A recently completed randomized crossover experiment found that the postprandial glycemic response to beverages that ranked high on the glycemic index (GI) (in this case, beverages containing large amounts of sucrose and isomaltulose) was significantly greater in individuals with CLBP than in healthy, pain-free controls (7). Moreover, the postprandial glycemic response to sucrose in the CLBP group was associated with greater pain severity and pain interference, underscoring clinical significance of the response (7). In contrast, no significant differences between groups were found in the postprandial glycemic response to a low-GI beverage (7).

In this paper, we report on a secondary analysis of the previously mentioned study to identify lifestyle-related factors that may predict impaired blood glucose regulation in individuals with CLBP. This additional analysis is driven by separate observations linking lifestyle factors to blood glucose regulation and pain intensity (8-10). Despite the potential impact on treatment, there is currently no evidence linking these elements to eachother in cases of CLBP. While the precise mechanisms underlying the relationship between chronic pain and altered glucose metabolism are not fully understood, existing evidence suggests that dysfunctional glucose processing may contribute to the persistence and exacerbation of chronic pain (7,11). Indeed, elevated glucose levels can promote central nervous system sensitization via the upregulation of high mobility group protein B1, which modulates inflammatory responses in the neurons of the dorsal root ganglia (12). Moreover, the glucocorticoid system is proposed as a mediator linking inflammation, glucose metabolism, and pain (13). Lifestyle factors and glucose metabolism show well-established links to body composition and glucose dysregulation (14). There is evidence regarding the influence of lifestyle factors such as physical activity on glucose metabolism, blood glucose regulation, and insulin resistance (15-17). Furthermore, psychological distress can disrupt the hypothalamic-pituitary-adrenal axis, influencing glycemic control and contributing to the development of metabolic syndrome (18,19).

Objectives

By examining the potential predictive role of lifestyle factors in impaired glucose regulation among individuals with CLBP, this study aims to integrate these observations into a unified analysis, contributing to a more comprehensive understanding of how lifestyle modifications may influence metabolic responses and pain management in CLBP patients. Specifically, this study aimed to characterize glycemic response patterns following sucrose intake, focusing on both the total postprandial glucose response and dynamic changes in blood glucose levels over time. We sought to accomplish 2 goals: Our first was to examine the relationship between predictor variables and the overall glycemic response, measured by the incremental area under the curve (IAUC). Our second was to use linear mixed models (LLMs) to assess the temporal changes in blood glucose levels immediately after sucrose intake. This dual approach was intended to enable a nuanced understanding of both the cumulative and immediate impacts of sucrose intake on glycemic control, facilitating insights into personalized management strategies for mitigating glycemic variability. While no evidence on this topic is currently available, this paper aims to add guidance regarding the impact of lifestyle factors on the underlying mechanisms of chronic pain through glucose metabolism and the possibility that these factors may be effective prevention options.

Methods

Study Design and Setting

This study is a secondary analysis using the data from a case-control randomized controlled crossover trial (Clinicaltrials.gov NCT04459104) conducted at Vrije Universiteit Brussel, Belgium. Data collection took place between September 2020 and December 2022. The study was approved by the Medical Ethics Committee of the University Hospital Brussels (BUN1432020000025). Full details of the trial design and primary analysis are available (7,24). Fig. 1 represents the flow of the study design.

Patients and Sample Size

A sample of female patients (n = 106) was recruited through posters and fliers. Patients were eligible if they spoke Dutch and were between 18 and 65 years of age. For the patients, CLBP was defined as a state of experiencing LBP at least 3 days per week for least 3 months. Patients with CLBP were excluded if they suffered from a systemic or cardiovascular disease, neuropathic or chronic widespread pain, or a specific spinal pathology. The potential presence of neuropathic pain was evaluated using the DN4 and SLANSS questionnaires (25,26). The control group included pain-free, healthy women. To ensure the accuracy and reliability of the pain measurements, neither the patients nor the healthy controls could consume analgesics, nicotine, caffeine, or alcohol for 48 hours before the experimental pain assessments.

Procedure and Measurements

Prior to any data collection, all patients read and signed the consent form. First, the answers to the DN4

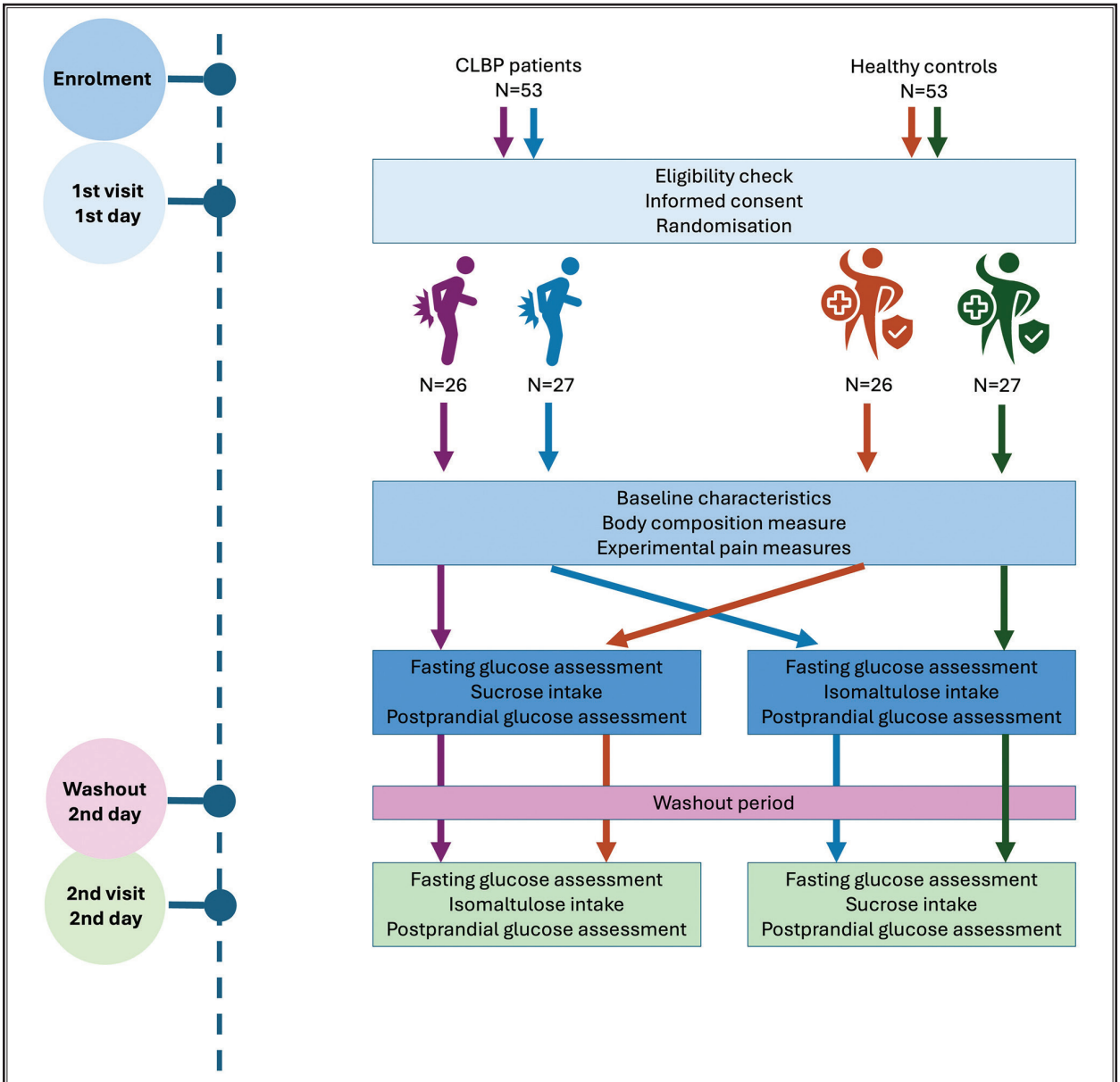

Fig. 1. *Flow of the study design (created with BioRender.com, accessed on 02/26/2024). From Elma et al (7).*

and SLANSS questionnaires and data on body composition were collected. A bioelectrical impedance analysis device (TANITA MC780MA, Antares Group) was used to measure body composition. Outcomes included body weight, body height (measured with a seca® scale), fat percentage, water percentage, and body mass index (BMI) (27). TANITA has good psychometric properties for measuring body composition (28).

Afterward, the patients' fasting blood glucose levels and postprandial glycemic responses were measured with a OneTouch Verio™ device (LifeScan, Inc.). OneTouch Verio™ uses a finger prick to collect a blood sample, which can be used independently by people who have no medical training (29,30). Patients were asked to visit the lab in the morning after an overnight fast of 10-12 hours and were allowed to ingest only water ad libitum. Two fasting blood samples were obtained 5 minutes apart to determine each patient's fasting blood glucose level. An additional fasting blood sample was taken if the first 2 were more than 0.2 mmol/L apart (31,32). The mean value was used in the analyses.

The procedure for measuring the postprandial glycemic response was based on a study by Tan et al (32) and was conducted as a crossover trial design over 2 nonconsecutive test days. Patients were given test beverages containing 50 gr of isomaltulose (low GI = 32) or 50 gr of sucrose (high GI = 65) dissolved in 250 mL of water in a random order. The patients were instructed to consume these beverages within 5 minutes. Blood glucose levels were collected at 15, 30, 45, 60, 90, and 120 minutes after the consumption of the beverages. Each time, the first 2 drops of blood were discarded, and the third drop was used for testing.

At the end of the session, each patient received a food diary in which to record her dietary intake for 3 days. The assessor provided the patients with clear instructions on completing the diary within 2 weeks after the assessment session. From the data collected via the food diary, dietary intake levels and scores on the Healthy Eating Index (HEI) and Dietary Inflammatory Index (DII) were calculated. The remaining information was gathered through online questionnaires. Patients were required to document their physical activity on the International Physical Activity Questionnaire (IPAQ) and their quality of life and demographic details, including age and symptom duration, on the 36-Item Short-Form Health Survey (SF-36) questionnaire. The IPAQ has moderate-to-high validity (33), while the SF-36 is a useful tool with high sensitivity (84.4%) and specificity (93.3%) as a predictor value of mental health issues (34).

Selection of Predictors and Their Rationale for Selection

Body Composition

The relationship between body weight and glucose metabolism is clear and widely described in the literature (14). Obesity is the most significant risk factor for the development of prediabetes and type 2 diabetes (35). Moreover, compared to people with normal weight, diabetic patients with (pre-)obesity showed higher blood glucose levels (36). In this study, BMI and fat mass percentage were measured to define the profiles of the patients.

Diet Ingesta

Diet has a direct impact on the risk of developing insulin resistance. Although diet can be protective when the intake of fruits, vegetables, or healthy fats (e.g., linoleic acid) is adequate, it can also be a risk factor, such as when the patient ingests saturated fat excessively (14). Specifically, the excessive consumption of processed meat has been linked with increased risks of hyperglycemia and hyperinsulinemia, while a diet rich in fruits or vegetables is beneficial for cardiovascular health and can decrease the prevalence of type 2 diabetes and metabolic syndrome (37,38). Diet was included in the analysis through the use of the HEI, with a specific focus on the patients' consumption of vegetables, fruits, and meat.

Furthermore, the impact of alcohol on glucose metabolism remains complex and not fully understood, influenced by multiple variables, including the dosage, the timing of consumption relative to meals, and whether the intake is acute or chronic. Evidence suggests that alcohol consumption can alter insulin secretion, potentially exacerbating glucose intolerance and elevating plasma glucose levels when consumed habitually (39,40). To quantify their alcohol intake, patients were queried about their consumption, which was measured in grams.

Healthy Eating Index (HEI)

The HEI questionnaire is a measure of diet quality. A higher index indicates better diet quality (41). The link between HEI and various health conditions has been established in the literature; for instance, a lower score on the HEI is inversely associated with BMI and

obesity (42), and an improvement in HEI is associated with a decreased risk of the development of metabolic diseases such as prediabetes (43).

Dietary Inflammatory Index (DII)

The DII is a dietary index that classifies food based on its impacts on major inflammatory biomarkers. Each component is scored based on its inflammatory or anti-inflammatory effects. These scores are standardized and added up to produce a total DII score. The higher the final score, the greater the pro-inflammatory properties of the diet (44). Higher scores have been related to obesity, metabolic syndrome, cardiovascular diseases, increased risk of cancer, adverse mental health, and musculoskeletal disorders (45,46).

Physical Activity

Physical activity can not only alter the risk of developing diabetes but can also enhance glycemic control markers, which is essential for both prevention and treatment (15,39,48). Studies show an inverse association between the level of physical activity and alterations in blood glucose levels (48). Moreover, the same association was found in patients who engaged in mild or moderate physical activity (49).

Psychological Factors

Self-percieved general mental health was measured using the SF-36. In this secondary analysis, we focused particularly on the subscale of mental health (50), since it showed statistically significant differences between healthy controls and CLBP patients and a link with glycemic response (24). Moreover, other authors also show associations between glycemic variability and depression in patients (51).

Glycemic Response

Fluctuations in glycemic control have been associated with the risk of the development of type 2 diabetes and complications in patients without diabetes (48). This secondary data analysis included the blood glucose levels at the baseline and 60 minutes after the intake of the sucrose, as well as the positive IAUC of the postprandial glucose response to the sucrose beverage. The latter was determined by excluding the area under the fasting blood glucose level (52). This calculation was made using the Python programming language (Python 3.8). (See Appendix 1 for the corresponding source code.) The outcome measure was the glycemic response.

Statistical Analyses

Data were analyzed using IBM SPSS Statistics 28.0 (SPSS Corp). Baseline characteristics and demographics were reported using mean and standard deviation (SD), median and interquartile range (IQR), and frequencies (%). The normality of the data was assessed using the Kolmogorov-Smirnov test (KS), and *P*-values < 0.05 were considered statistically significant.

Firstly, multiple linear regression analysis was utilized to examine the relationship between various predictor variables and the outcome variable, i.e., IAUC of the postprandial glucose response. Initially, a backward regression approach was employed to eliminate non-significant predictor variables from the model, based on a predetermined significance level ($P < 0.05$ for entry and $P > 0.10$ for removal), and the variance inflation factor (VIF) was used to check for multicollinearity. Additionally, residual plots, including histograms and normal probability plots, were generated to evaluate the assumptions of linear regression.

Secondly, an LMM was used to assess how blood glucose levels responded over time, particularly from the baseline to 60 minutes after the sucrose intake, while accounting for the influence of individual and group-level factors. Unlike the first analysis, which focused on the total postprandial glucose response captured by the IAUC, this analysis specifically examined fluctuations in blood glucose at those 2 critical time points. This approach was valuable because it allowed us to capture dynamic changes in blood glucose in response to sucrose intake, providing a detailed understanding of the immediate glycemic response. By employing an LMM, we were able to incorporate random effects to account for individual-level variability as well as fixed effects, like time and group interactions. Each step of the analysis served to address the variability and complexity of the blood glucose response comprehensively. Univariate analysis was used as an initial filter to identify significant predictors, which established the most relevant variables. Multivariable model refinement based on Akaike information criterion and Bayesian information criterion allowed us to create a parsimonious model that adequately explained the variance in blood glucose changes. Model fit measures (ICCs and pseudo-R^2) and model diagnostics ensured that the model accurately captured underlying patterns and temporal changes in blood glucose while addressing differences among the patients.

Results

One patient from the CLBP group was deleted

from the database because she did not return the food diary. Therefore, a total sample size of 105 people was examined, including 53 healthy controls and 52 CLBP patients. Sample characteristics can be found in Table 1. The 2 groups did not differ significantly at the baseline in age, weight, height, or body fat percentage. The CLBP group had significantly lower HEI scores, indicating poorer diet quality compared to healthy controls ($P = 0.01$). Additionally, the patients in the CLBP group had more inflammatory diets, as reflected by a higher DII ($P = 0.003$). Mental health scores were better in the healthy controls ($P = 0.026$). The CLBP patients were more physically active, according to the moderate activity subscale of the IPAQ ($P = 0.005$). Lastly, healthy controls had a higher vegetable intake than the CLBP patients did ($P = 0.010$). Neither meat intake nor fruit intake was associated with differences between CLBP patients and healthy controls. Although the group differences in this variable are noteworthy, alcohol intake was similarly not associated with significant differences between groups.

The regression analysis revealed significant associations between several predictor variables and the outcome variable (postprandial glucose response) in the multivariable model ($F(7,97) = 7.597$, $P < 0.001$, adjusted $R^2 = 0.307$). Individuals with CLBP had significantly higher postprandial glycemic response scores (in response to sucrose) than did healthy controls ($P = 0.002$). Age ($P = 0.003$), weight ($P < 0.001$), and DII ($P = 0.025$) were directly associated with the postprandial glycemic response in patients with CLBP. Mental health ($P = 0.021$), HEI scores ($P = 0.002$), and total fruit component scores on the aforementioned index ($P = 0.016$) were also significantly associated with the outcome variable (Table 2). The syntax can be found in Appendix 2.

The LMM analysis revealed that the glycemic response after sucrose intake exhibited a significant positive association with time (estimate = 26.08, 95% CI (17.43, 32.73), $P < 0.001$), indicating an increase in glycemic glucose response over time (60 minutes). The group variable (CLBP) did not affect the outcome significantly ($P = 0.111$). Weight had a small but significant positive effect (estimate = 0.15, 95% CI (0.01, 0.28), $P = 0.035$), while the effect of fruit consumption was not significant (estimate = 0.93, 95%CI (-0.10, 1.97), $P = 0.075$). For the CLBP patients, the interaction between time and group was not significant (estimate = 8.20, 95% CI (-1.25, 17.66), $P = 0.088$). The estimates of covariance parameters indicated a residual variance of 3.88 (SE = 23.13, $P = 0.867$), an intercept variance of 83.24 (SE = 25.91, $P = 0.001$), and a time variance of 588.90 (SE = 94.19, $P < 0.001$). The adjusted model's intraclass correlation coefficient was 0.990, indicating that a substantial proportion of the variance was attributable to between-subject differences. The marginal pseudo-R^2 was 0.387, suggesting that the fixed effects accounted for approximately 38.7% of the variance, while the conditional pseudo-R^2 was 0.994, indicating that the full model, including both fixed and random effects, accounted for 99.4% of the variance (Table 3). The syntax can be found in Appendix 3.

Discussion

This secondary analysis investigated the association of several lifestyle-related factors and an altered glycemic response in people suffering from CLBP. Results suggested that weight ($P < 0.001$; t = -4.06), higher age ($P = 0.003$; t = 3.06), higher inflammatory dietary properties ($P = 0.025$; t = 2.28), lower mental health ($P = 0.021$; t = 2.34) and lower diet quality ($P = 0.002$; t = 3.22) had a significant predictive value for altered postprandial sucrose responses.

These findings in patients with CLBP confirm findings of earlier studies that have shown how lifestyle-related factors such as dietary habits, physical activity, or gut microbiome composition can potentially predict postprandial glycemic responses in healthy people (53). Indeed, in an 800-person cohort (60% female; age: mean ± SD = 43.3 ± 13.1; BMI = 26.4 ± 5.1), fasting glucose levels, BMI, and age were significant risk factors associated with postprandial glycemic response, showing similarities to the roles of body composition (although not reported as BMI in the present study) and age reported in our study. Importantly, this study concluded that the postprandial glycemic response among the sample of CLBP patients was highly variable, despite the consumption of the same meals (53).

Chronic pain has been associated previously with other cardiovascular diseases and metabolic alterations (19). Goodson et al showed that patients who presented more pain intensity were associated with metabolic syndrome. This factor contributes to the development of insulin resistance and elevated blood glucose (19). Additionally, it has been suggested that for obese women, the increasing frequency of elevated pain, higher blood glucose levels, and chronic pain was significantly correlated with higher fasting glucose levels (18). Results have shown that a healthful diet, particularly the consumption of fruits and vegetables,

may be considered a possible protective factor against CLBP. However, neither meat nor alcohol was a significant predictor in the present study. A systematic review and meta-analysis of randomized controlled trials did not find any indication that red meat consumption was a glycemic risk factor for the development of type 2 diabetes (54). Meanwhile, attempts to monitor the influence of alcohol intake on glycemic control and insulin action have also shown unclear results (40). Therefore, those previous results are confirmed by those of the present study.

Table 1. *Sample characteristics of CLBP patients and healthy controls (n = 105).*

	CLBP (n = 52) Mean (SD)	HC (n = 53) Mean (SD)	Effect Size (Cohen's d)	*P*-value
Age	37.1 (12.7)	34.1 (9.8)	0.26	0.179
Weight (kg)	71.6 (15.0)	69.7 (12.1)	0.14	0.474
Height (cm)	163.3 (5.8)	164.6 (7.1)	-0.19	0.328
BMI (kg/m^2)	26.9 (6.0)	25.8 (4.9)	0.20	0.313
Body fat mass%	32.5 (7.0)	31.8 (6.8)	0.11	0.572
HEI	55.1 (14.9)	61.5 (9.6)	−0.51	0.010*
DII	2.0 (1.6)	1.0 (1.6)	0.59	0.003*
Mental health (SF-36)	61.6 (20.6)	69.7 (15.6)	−0.44	0.026*
Physical activity (moderate MET on IPAQ)	2,463.3 (2,679.3)	1,315.0 (1,060.3)	0.57	0.005*
Meat ingesta (saturated fats component of HEI)	4.54 (2.9)	3.60 (2.9)	0.326	0.862
Fruit ingesta (total fruit component of HEI)	3.59 (1.8)	3.48 (1.8)	0.65	0.931
Vegetable ingesta (total vegetable component of HEI)	3.86 (1.3)	4.66 (0.7)	-0.073	0.010*
Alcohol ingesta (gr)	2.94 (7.1)	1.29 (4.4)	0.279	0.071

Abbreviations: n = number of patients; SD = standard deviation; kg = kilogram; cm = centimeter; BMI = body mass index; m = meter; IPAQ = International Physical Activity Questionnaire; MET = Metabolic Equivalent of Task; HEI = Healthy Eating Index, with a maximum score of 100, reflecting the best diet quality; DII = Dietary Inflammatory Index, with 0 being the healthiest score; SF-36 = 36-Item Short-Form Health Survey, with a maximum score of 100, reflecting the best quality of life; gr = grams.

Mental health was also associated with the postprandial glucose response. This connection confirmed observations by other authors, who have shown the importance of this variable in individuals who suffer from altered glycemic response and pain. "Patients tend to have worse physical functioning and mental health than individuals without pain" (55). Mental health issues such as depression have been reported in chronic pain conditions as a bidirectional association and established as a predictor of chronicity (56). Lastly, physical activity has been reported massively as a protective factor in glycemic control, as part of the prevention of altered glucose response and also part of the solution when diseases such as diabetes develop (48,57,58). Physical activity "is an effective, cheap, and safe therapeutic option, given that it does not produce the adverse effects of pharmacological treatments or invasive techniques" (59).

Table 2. *Regression coefficients for predictors of postprandial glucose response after sucrose intake (IAUC) in individuals with chronic low back pain (CLBP).*

Variables	Estimates	Std. Error	t	*P* value
Intercept	1471.25	926.81	1.587	0.116
Group (CLBP)	786.45	248.14	3.169	0.002*
Age (years)	32.90	10.75	3.06	0.003*
Weight (kg)	-35.56	8.77	-4.056	< 0.001*
Mental health	15.02	6.41	2.344	0.021*
DII	167.16	73.22	2.283	0.025*
HEI	35.30	10.98	3.215	0.002*
Total fruit component on HEI	-184.89	75.43	-2.451	0.016*
R-squared				
Adjusted	0.307			

Abbreviations: CLBP = chronic low back pain; kg = kilograms, DII = Dietary Inflammatory Intake; HEI = Healthy Eating Index 2015.

It is important to highlight the clinical relevance of the results of this study. From a clinical perspective, we must consider the factors and lifestyle habits that we can modify in patients with chronic pain (9). The evidence for the relationship between neuroinflammation and pain has grown increasingly strong (21); therefore, we should address as many factors as possible to create the most comprehensive rehabilitation program. Furthermore, the lifestyle-related approaches (diet, physical activity, and mental health) have been shown to be more effective in the regulation of altered glucose response when used together than when used separately (60).

Although research on the metabolic topic of chronic pain conditions has expanded significantly

Table 3. *LMM summary of fixed effects, covariance parameters, ICCs, and pseudo-R-squared measures.*

Parameter	Estimate	95% CI	Std. Error	*P* value
Fixed effects				
Intercept	83.52	(73.63; 93.40)	4.98	< 0.001
Time	26.08	(17.43; 32.73)	3.36	< 0.001
Group (CLBP)	-2.94	(-6.56; 0.69)	1.83	0.111
Weight	0.15	(0.01; 0.28)	0.07	0.035
HEIC3TOTFRUIT	0.93	(-0.10; 1.97)	0.52	0.075
Time*Group (CLBP)	8.20	(-1.25; 17.66)	4.77	0.088
Estimates of Covariance Parameters				
Residual	3.88		23.13	0.867
Intercept variance	83.24		25.91	0.001
Time variance	588.90		94.19	< 0.001
ICC				
Adjusted	0.990			
Conditional	0.607			
Pseudo-R-Square Measures				
Marginal	0.387			
Conditional	0.994			

Note: ICC = intraclass correlation coefficient, time (0 = sucrose 0', 1 = Sucrose 60'), group (0 = healthy controls, 1 = CLBP patients).

in recent years, only a limited number of biomarkers have been confirmed as reliable for pain management (61). Considering the widespread prevalence of chronic pain, there is a critical need for metabolic biomarkers that can help in predicting, diagnosing, and managing chronic pain disorders (22). Therefore, the research on biomarkers should also be conducted with psychological and functional characteristics in mind, to enhance their clinical utility and to find accurate predictors for chronic pain (62). Because postprandial glucose response has been previously associated with chronic pain, incorporating knowledge of the aforementioned characteristics could represent a novel therapeutic approach and a potential area of focus for future research on chronic pain treatment.

According to our results, reducing body weight, improving mental health, and changing to a healthier diet with increased fruit intake could be key factors in enhancing the prognosis of patients with chronic pain.

Limitations

Some limitations of the present study should be considered. First, this study is a secondary analysis of the case-control sub-study of an experimental crossover trial, so we must be careful in making causal interpretations. Postprandial glucose response was measured by the researchers' use of a self-monitoring device requiring the pricking of the patients' fingers; although this method is the most common for monitoring capillary blood glucose levels, it does not provide the necessary information to capture blood glucose fluctuations in real-time settings. Moreover, while this highly feasible, easily accessible method for measuring glucose levels was advantageous, its use meant that insulin levels could not be assessed simultaneously. Not integrating insulin sensitivity and resistance constrained our ability to develop a more extensive and comprehensive model. Finally, all the patients in this study were women, so our findings may not be applicable to men.

However, though the dietary reports collected for the study might have introduced recall bias, social desirability bias, and possible under- or overestimating of dietary intake (depending on the food product), the process of measuring food consumption over a 3-day period is recognized for its accuracy and ability to minimize those biases. As for the glucose response, our study measured the fasting glucose levels up to one hour after the intake of the sucrose. Although measuring glucose levels 2 hours after the intake is common in the literature (11), doing so one hour after the intake has been presented as a sensitive alternative, with great specificity and sensitivity (63). The one-hour test is also a good substitute, since it reduces the cost and time of screening and can predict type 2 diabetes and its complications and mortality (63). An important difference between our study and others is our use of more detailed body composition (18,53). In our study, we selected fat percentages as body composition outcomes because of the known limitations in the accuracy of BMI to represent body composition (64,65).

Conclusions

This secondary analysis rigorously explored various predictor variables potentially associated with altered glycemic responses in patients with CLBP. The study confirmed that higher weight, age, and quantities of inflammatory dietary properties were associated with a significant predictive value for altered postprandial sucrose responses, as were lower qualities of mental

health and diet. The implications of these results underscore the paramount importance of lifestyle habits in the management of glucose levels and contribute to a deeper understanding of the metabolic responses in CLBP patients. Early management of those lifestyles could potentially prevent the metabolic alterations observed in patients with chronic pain.

Author Affiliations

[1]Escuela internacional de Doctorado, Rey Juan Carlos University, Madrid, Spain; [2]Department of Physical Therapy, Occupational Therapy, Rehabilitation and Physical Medicine, Rey Juan Carlos University, Madrid, Spain; [3]Cognitive Neuroscience, Pain, and Rehabilitation Research Group (NECODOR), Faculty of Health Sciences, Rey Juan Carlos University, Madrid, Spain; [4]UNIE Universidad, Madrid, Spain; [5]Physiotherapy Unit, Department of Rehabilitation and Sport Sciences, Faculty of Health and Social Sciences, Bournemouth University, Bournemouth, UK; [6]Movement and Nutrition for Health and Performance (MOVE) Research Group, Department of Movement and Sport Sciences, Faculty of Physical Education & Physiotherapy, Vrije Universiteit Brussel, Brussels, Belgium; [7]Pain in Motion Research Group (PAIN), Department of Physiotherapy, Human Physiology and Anatomy, Faculty of Physical Education and Physiotherapy, Vrije Universiteit Brussel, Brussels, Belgium; [8]Core Facility - Support for Quantitative and Qualitative Research (SQUARE), Vrije Universiteit Brussel (VUB), Brussels, Belgium; [9]Department of Physiotherapy, Human Physiology and Anatomy, Faculty of Physical Education and Physiotherapy, Vrije Universiteit Brussel, Brussels, Belgium; [10]Department of Physiotherapy, Faculty of Sport Sciences, Universidad Europea de Madrid, Villaviciosa de Odón, Spain; [11]Chronic Pain Rehabilitation, Department of Physical Medicine and Physiotherapy, University Hospital, Brussels, Belgium; [12]Unit of Physiotherapy, Department of Health and Rehabilitation, Institute of Neuroscience and Physiology, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden; [13]Research Foundation Flanders (FWO), Brussels, Belgium

Supplemental material is available at www.painphysicianjournal.com

References

1. Clark JD, Bair MJ, Belitskaya-Lévy I, et al. Sequential and Comparative Evaluation of Pain Treatment Effectiveness Response (SCEPTER), a pragmatic trial for conservative chronic low back pain treatment. *Contemp Clin Trials* 2023; 125:107041.
2. Pillastrini P, Ferrari S, Rattin S, Cupello A, Villafañe JH, Vanti C. Exercise and tropism of the multifidus muscle in low back pain: A short review. *J Phys Ther Sci* 2015; 27:943–945.
3. Saragiotto BT, Machado GC, Ferreira ML, Pinheiro MB, Abdel Shaheed C, Maher CG. Paracetamol for low back pain. *Cochrane Database Syst Rev* 2016; 2016:CD012230.
4. Balagué F, Mannion AF, Pellisé F, Cedraschi C. Non-specific low back pain. *Lancet* 2012; 379:482-491.
5. Mauck MC, Aylward AF, Barton CE, et al. Evidence-based interventions to treat chronic low back pain: Treatment selection for a personalized medicine approach. *Pain Rep* 2022; 7:e1019.
6. Sanzarello I, Merlini L, Rosa MA, et al. Central sensitization in chronic low back pain: A narrative review. *J Back Musculoskelet Rehabil* 2016; 29:625-633.
7. Elma Ö, Tümkaya Yılmaz S, Nijs J, et al. Impaired carbohydrate metabolism among women with chronic low back pain and the role of dietary carbohydrates: A randomized controlled cross-over experiment. *J Clin Med* 2024; 13:2155.
8. Knowler WC, Barrett-Connor E, Fowler SE, et al. Diabetes prevention program research group reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *N Engl J Med* 2002; 346:393-403.
9. Nijs J, D'Hondt E, Clarys P, et al. Lifestyle and chronic pain across the lifespan: An inconvenient truth? *PM R* 2020; 12:410-419.
10. Gonzalez-Alvarez ME, Sanchez-Romero EA, Turroni S, Fernandez-Carnero J, Villafañe JH. Correlation between the altered gut microbiome and lifestyle interventions in chronic widespread pain patients: A systematic review. *Medicina (Kaunas)* 2023; 59:256.
11. Mäntyselkä P, Miettola J, Niskanen L, Kumpusalo E. Chronic pain, impaired glucose tolerance and diabetes: A community-based study. *Pain* 2008; 137:34-40.
12. Bestall SM, Hulse RP, Blackley Z, et al. Sensory neuronal sensitisation occurs through HMGB-1-RAGE and TRPV1 in high-glucose conditions. *J Cell Sci* 2018; 131: jcs215939.
13. Sim YB, Park SH, Kang YJ, et al. Interleukin-1β (IL-1β) increases pain behavior and the blood glucose level: Possible involvement of glucocorticoid system. *Cytokine* 2013; 64:351-356.
14. van Dam RM, Willett WC, Rimm EB, Stampfer MJ, Hu FB. Dietary fat and meat intake in relation to risk of type 2 diabetes in men. *Diabetes Care* 2002; 25:417-424.
15. Schubert-Olesen O, Kröger J, Siegmund T, Thurm U, Halle, M. Continuous glucose monitoring and physical activity. *Int J Environ Res Public Health* 2022; 19:12296.
16. Reik A, Brandl B, Schauberger G, et al. Association between habitual diet and the postprandial glucose response-An Enable study. *Mol Nutr Food Res* 2022; 66:e2200110.
17. Oba-Yamamoto C, Takeuch J,

Nakamura A, et al. Combination of alcohol and glucose consumption as a risk to induce reactive hypoglycemia. *J Diabetes Investig* 2021; 12:651–657.

18. Burns JW, Quartana PJ, Bruehl S, et al. Chronic pain, body mass index and cardiovascular disease risk factors: Tests of moderation, unique and shared relationships in the Study of Women's Health Across the Nation (SWAN). *J Behav Med* 2015; 38:372–383.
19. Goodson NJ, Smith BH, Hocking LJ, et al. Cardiovascular risk factors associated with the metabolic syndrome are more prevalent in people reporting chronic pain: Results from a cross-sectional general population study. *Pain* 2013; 154; 1595-1602.
20. Boer CG, Radjabzadeh D, Medina-Gomez C. Intestinal microbiome composition and its relation to joint pain and inflammation. *Nat Commun* 2019; 10:4881.
21. Nijs J, Elma Ö, Yilmaz ST, et al. Nutritional neurobiology and central nervous system sensitisation: Missing link in a comprehensive treatment for chronic pain? *Br J Anaesth* 2019; 123:539–543.
22. Aroke EN, Powell-Roach KL. The metabolomics of chronic pain conditions: A systematic review. *Biol Res Nurs* 2020; 22:458-471.
23. González-Álvarez ME, Riquelme-Aguado V, González-Pérez Á, et al. Association between systemic neuroinflammation, pain perception and clinical status in fibromyalgia patients: Cross-sectional study. *Cells* 2024; 13:1719.
24. Elma Ö, Tümkaya Yılmaz S, Nijs J, et al. Proinflammatory dietary intake relates to pain sensitivity in chronic nonspecific low back pain: A case-control study. *J Pain* 2024; 25:350–361.
25. Bennett MI, Smith BH, Torrance, N, Potter, J. The S-LANSS score for identifying pain of predominantly neuropathic origin: Validation for use in clinical and postal research. *J Pain* 2005; 6:149-158.
26. Epping R, Verhagen AP, Hoebink EA, Rooker S, Scholten-Peeters, GGM. The diagnostic accuracy and test-retest reliability of the Dutch PainDETECT and the DN4 screening tools for neuropathic pain in patients with suspected cervical or lumbar radiculopathy. *Musculoskelet Sci Pract* 2017; 30:72–79.
27. Thivel D, Verney J, Miguet M, et al. The accuracy of bioelectrical impedance to track body composition changes depends on the degree of obesity in adolescents with obesity. *Nutr Res* 2018; 54:60068.
28. Vasold KL, Parks AC, Phelan DML, Pontifex MB, Pivarnik JM. Reliability and validity of commercially available low-cost bioelectrical impedance analysis. *Int J Sport Nutr Exerc Metab* 2019; 29:406-410.
29. Bailey T, Chang A, Rosenblit PD, et al. A comprehensive evaluation of the performance of the test strip technology for OneTouch Verio glucose meter systems. *Diabetes Technol Ther* 2012; 14:701-709.
30. Littmann K, Petersen ERB, Pussinen C, et al. Evaluation of OneTouch Verio(®), a new blood glucose self-monitoring system for patients with diabetes. *Scand J Clin Lab Invest* 2013; 73:286-292.
31. Lilly LN, Heiss CJ, Maragoudakis SF, Braden KL, Smith SE. The effect of added peanut butter on the glycemic response to a high-glycemic index meal: A pilot study. *J Am Coll Nutr* 2019; 38:351-357.
32. Tan WSK, Tan SY, Henry CJ. Ethnic variability in glycemic response to sucrose and isomaltulose. *Nutrients* 2017; 9:347.
33. Sember V, Meh K, Sorić M, Starc G, Rocha P, Jurak G. Validity and reliability of international physical activity questionnaires for adults across EU countries: Systematic review and meta analysis. *Int J Environ Res Public Health* 2020; 17:7161.
34. Elliott TE, Renier CM, Palcher JA. Chronic pain, depression, and quality of life: Correlations and predictive value of the SF-36. *Pain Med* 2003; 4:331-339.
35. Barnes AS. The epidemic of obesity and diabetes: Trends and treatments. *Tex Heart Inst J* 2011; 38:142-144.
36. Patel BJ, Mehta DN, Vaghani A, Patel K. Correlation of body mass index (BMI) with saliva and blood glucose levels in diabetic and non-diabetic patients. *J Pharm Bioallied Sci* 2023; 15:S1204-S1207.
37. Gu X, Drouin-Chartier JP, Sacks FM, Hu FB, Rosner B, Willett WC. Red meat intake and risk of type 2 diabetes in a prospective cohort study of United States females and males. *Am J Clin Nutr* 2023; 118:1153-1163.
38. Panagiotakos DB, Tzima N, Pitsavos C, et al. The relationship between dietary habits, blood glucose and insulin levels among people without cardiovascular disease and type 2 diabetes; the ATTICA study. *Rev Diabet Stud* 2005; 2:208-215.
39. Russell WR, Baka A, Björck I, et al. Impact of diet composition on blood glucose regulation. *Crit Rev Food Sci Nutr* 2016; 56:541-590.
40. Steiner JL, Crowell KT, Lang CH. Impact of alcohol on glycemic control and insulin action. *Biomolecules* 2015; 5:2223-2246.
41. Krebs-Smith SM, Pannucci TE, Subar AF, et al. Update of the Healthy Eating Index: HEI-2015. *J Acad Nutr Diet* 2018; 118:1591-1602.
42. Zhao Y, Araki T. Diet quality and its associated factors among adults with overweight and obesity: Findings from the 2015-2018 National Health and Nutrition Examination Survey. *Br J Nutr* 2024; 131:134–142.
43. Costello E, Goodrich J, Patterson WB, et al. Diet quality is associated with glucose regulation in a cohort of young adults. *Nutrients* 2022; 14:3734.
44. Hébert JR, Shivappa N, Wirth MD, Hussey JR, Hurley TG. Perspective: The Dietary Inflammatory Index (DII)—Lessons learned, improvements made, and future directions. *Adv Nutr Bethesda Md* 2019; 10:185-195.
45. Motamedi A, Askari M, Mozaffari H, et al. Dietary Inflammatory Index in relation to type 2 diabetes: A meta-analysis. *Int J Clin Pract* 2022; 2022:9953115.
46. Phillips CM, Chen LW, Heude B, et al. Dietary Inflammatory Index and non-communicable disease risk: A narrative review. *Nutrients* 2019; 11:1873.
47. Kim Y, Chen J, Wirth MD, Shivappa N, Hebert JR. Lower Dietary Inflammatory Index scores are associated with lower glycemic index scores among college students. *Nutrients* 2018; 10:182.
48. El Fatouhi D, Héritier H, Allémann C, et al. Associations between device-measured physical activity and glycemic control and variability indices under free-living conditions. *Diabetes Technol Ther* 2022; 24:167-177.
49. Kingsnorth AP, Whelan ME, Sanders JP, Sherar LB, Esliger DW. Using digital health technologies to understand the association between movement behaviors and interstitial glucose: Exploratory analysis. *JMIR MHealth UHealth* 2018; 6:e114.
50. Aaronson NK, Muller M, Cohen PD, et al. Translation, validation, and norming of the Dutch language version of the SF-36 Health Survey in community and chronic disease populations. *J Clin Epidemiol* 1998; 51:1055-1068.
51. Marchini F, Caputo A, Convertino A, et al. Associations between continuous

glucose monitoring (CGM) metrics and psycholinguistic measures: A correlational study. *Acta Diabetol* 2024; 61:841-845.

52. Wolever TM. Effect of blood sampling schedule and method of calculating the area under the curve on validity and precision of glycaemic index values. *Br J Nutr* 2004; 91:295-301.
53. Zeevi D, Korem T, Zmora N, et al. Personalized nutrition by prediction of glycemic responses. *Cell* 2015; 163:1079-1094.
54. Sanders LM, Wilcox ML, Maki KC. Red meat consumption and risk factors for type 2 diabetes: A systematic review and meta-analysis of randomized controlled trials. *Eur J Clin Nutr* 2023; 77:156-165.
55. Todd J, Rudaizky D, Clarke P, Sharpe L. Cognitive biases in type 2 diabetes and chronic pain. *J Pain* 2022; 23:112-122.
56. Ang DC, Bair MJ, Damush TM, Wu J, Tu W, Kroenke K. Predictors of pain outcomes in patients with chronic musculoskeletal pain co-morbid with depression: Results from a randomized controlled trial. *Pain Med* 2010; 11:482–491.
57. Sparks JR, Kishman EE, Sarzynski MA, Davis JM, Grandjean PW, Durstine JL, Wang X. Glycemic variability: Importance, relationship with physical activity, and the influence of exercise. *Sports Med Health Sci* 2021; 3:183-193.
58. Syeda USA, Battillo D, Visaria A, Malin SK. The importance of exercise for glycemic control in type 2 diabetes. *Am J Med Open* 2023; 9:100031.
59. De la Corte-Rodriguez H, Roman-Belmonte JM, Resino-Luis C, Madrid-Gonzalez J, Rodriguez-Merchan EC. The role of physical exercise in chronic musculoskeletal pain: Best medicine—A narrative review. *Healthcare (Basel)* 2024; 12:242.
60. Yates T, Khunti K, Bull F, Gorely T, Davies MJ. The role of physical activity in the management of impaired glucose tolerance: A systematic review. *Diabetologia* 2007; 50:1116-1126.
61. Sluka KA, Wager TD, Sutherland SP, et al. Predicting chronic postsurgical pain: Current evidence and a novel program to develop predictive biomarker signatures. *Pain* 2023; 164:1912-1926.
62. Fillingim M, Tanguay-Sabourin C, Parisien M, et al. A biomarker-centric framework for the prediction of future chronic pain. *medRxiv*. Preprint. Posted online 04/20/2024. 2024; 2024.04.19.24306101.
63. Bergman M. The 1-hour plasma glucose: Common link across the glycemic spectrum. *Front Endocrinol (Lausanne)* 2021; 12:752329.
64. Frankenfield DC, Rowe WA, Cooney RN, Smith JS, Becker D. Limits of body mass index to detect obesity and predict body composition. *Nutrition* 2001; 17:26-30.
65. Nevill AM, Stewart AD, Olds T, Holder R. Relationship between adiposity and body size reveals limitations of BMI. *Am J Phys Anthropol* 2006; 129:151-156.

Appendix 1. *Description of the elements of the Python code and Python code for the calculation of the incremental area under the curve (IAUC).*

Line Number	Code Element	Description
2	Import module	"Import module" imports pandas and matplotlib libraries for required functions.
14	for loop	Iterates through the list containing all patients' data.
17	def areaUnderCurvelbpsu	Creates a function that calculates the area under the curve by using the trapezoidal rule, ignoring the values below fasting blood glucose level.
19	for loop	Iterates through the list that contains individual patient data.
20	If statement	If all the values are higher than the fasting blood glucose level, use this function to calculate the area of the trapezoid.
22	elif statement	If the first value is lower than the fasting blood glucose level and the second value is equal to or higher than the fasting blood glucose level, use this function to calculate the area of the trapezoid.
24	elif statement	If the first value is higher than or equal to the fasting blood glucose level and the second value is lower than the fasting blood glucose level, use this function to calculate the area of the trapezoid.
26	elif statement	If the fasting blood glucose level is higher than all the values, this function calculates the area of the trapezoid.
28	sum variable	The total sum of the area under the curve value for each individual.

```
1
2  import pandas as pd
3  import matplotlib.pyplot as plt
4
5  #Importing data from an excell file located in the local repository as a
   dataframe
6  lbisomaltulose = pd.read_excel("Local Directory Address",
   sheet_name="LBPISO")
7  lbsucrose = pd.read_excel("Local Directory Address", sheet_name="LBPSUC")
8  hcisomaltulose = pd.read_excel("Local Directory Address", sheet_name="HCISO'
9  hcsucrose = pd.read_excel("Local Directory Adress", sheet_name="HCSUC")
10 AUCLB = pd.read_excel("Local Directory Address", sheet_name = "AUCLB")
11
12 # For Loop and a user defined function for the calculation of incremental
   area under the curve for postprandial sucrose
13 # response of the low back pain patients
14 for i in range(len(lbsucrose.columns)):
15     a = [0, 15, 30, 45, 60, 90, 120]
16     b = lbsucrose.iloc[:, i]
17     def areaUnderCurvelbsuc(a, b):
18         sum = 0
19         for i in range(len(a) - 1):
20             if (b[i + 1] - b[0] >= 0) and (b[i] - b[0] >= 0):
21                 temp = ((b[i] - b[0] + b[i + 1] - b[0]) / 2) * (a[i + 1] -
   a[i])
22             elif (b[i + 1] - b[0] < 0) and (b[i] - b[0] >= 0):
23                 temp = (b[i] - b[0]) * ((b[i] - b[0]) / (b[i] - b[i + 1])) *
   (a[i + 1] - a[i]) / 2)
24             elif (b[i + 1] - b[0] >= 0) and (b[i] - b[0] < 0):
25                 temp = (b[i + 1] - b[0]) * ((b[i + 1] - b[0]) / (b[i + 1] -
   b[i]) * (a[i + 1] - a[i]) / 2)
26             elif (b[i] - b[0] < 0) and (b[i + 1] - b[0] < 0):
27                 temp = 0
28             sum = sum + temp
29         return round(sum)
30     print(areaUnderCurvelbsuc(a,b))
```

```
* Encoding: UTF-8.

DATASET ACTIVATE DataSet1.

# Univariate analysis with all variables and outcome
# Using backward regression

REGRESSION
  /MISSING LISTWISE
  /STATISTICS COEFF OUTS R ANOVA COLLIN TOL
  /CRITERIA=PIN(.05) POUT(.10) TOLERANCE(.0001)
  /NOORIGIN
  /DEPENDENT AUCSUCROSE
  /METHOD=BACKWARD AGE HEIGHT WEIGHT MUSPER FATPER SF36MH IPAQMODTOT DII HEI2015 HEIC1TOTVEG
    HEIC3TOTFRUIT HEIC12SFAT ALCDII5 LBP.

# Final model after removing insignificant variables.

REGRESSION
  /MISSING LISTWISE
  /STATISTICS COEFF OUTS R ANOVA COLLIN TOL
  /CRITERIA=PIN(.05) POUT(.10) TOLERANCE(.0001)
  /NOORIGIN
  /DEPENDENT AUCSUCROSE
  /METHOD=ENTER AGE WEIGHT SF36MH DII HEI2015 HEIC3TOTFRUIT LBP
  /PARTIALPLOT ALL
  /RESIDUALS HISTOGRAM(ZRESID) NORMPROB(ZRESID).
```

Appendix 2. *SPSS syntax for linear regression results.*

```
* Encoding: UTF-8.
DATASET ACTIVATE DataSet1.

# Random intercept model: AIC 1833.47 BIC 1840.15

MIXED sucrose WITH time1
  /CRITERIA=DFMETHOD(SATTERTHWAITE) CIN(95) MXITER(100) MXSTEP(10) SCORING(1)
    SINGULAR(0.000000000001) HCONVERGE(0.00000001, RELATIVE) LCONVERGE(0, ABSOLUTE) PCONVERGE(0,
    ABSOLUTE)
  /FIXED=time1 | SSTYPE(3)
  /METHOD=REML
  /PRINT= SOLUTION TESTCOV
  /RANDOM=INTERCEPT | SUBJECT(subID) COVTYPE(ID).

# Random intercept and random slopes AIC 1744.06 BIC 1754.08

MIXED sucrose WITH time1
  /CRITERIA=DFMETHOD(SATTERTHWAITE) CIN(95) MXITER(100) MXSTEP(10) SCORING(1)
    SINGULAR(0.000000000001) HCONVERGE(0.00000001, RELATIVE) LCONVERGE(0, ABSOLUTE) PCONVERGE(0,
    ABSOLUTE)
  /FIXED=time1 | SSTYPE(3)
  /METHOD=REML
  /PRINT= SOLUTION TESTCOV
  /RANDOM=INTERCEPT time1 | SUBJECT(subID) COVTYPE(VC).

# Univariate analysis, fit models 0.1 probability of entry, AGE, WEIGHT, MUSPER, FATPER, HEIC3TOTFRUIT were significant. LBP was not significant but we kept it in the model as it is a variable of interest
# The model was then fitted with significant variables and variables were removed at 0.05 level of significance also taking into account AIC and BIC values.

# Final model after variable selection

MIXED sucrose WITH time1 AGE HEIGHT WEIGHT MUSPER FATPER SF36MH IPAQMODTOT DII HEI2015 HEIC1TOTVEG
  HEIC3TOTFRUIT HEIC12SFAT ALCDII5 LBP
  /CRITERIA=DFMETHOD(SATTERTHWAITE) CIN(95) MXITER(100) MXSTEP(10) SCORING(1)
    SINGULAR(0.000000000001) HCONVERGE(0.00000001, RELATIVE) LCONVERGE(0, ABSOLUTE) PCONVERGE(0,
    ABSOLUTE)
  /FIXED=time1 LBP WEIGHT HEIC3TOTFRUIT time1*LBP | SSTYPE(3)
  /METHOD=REML
  /PRINT=SOLUTION TESTCOV
  /RANDOM=INTERCEPT time1 | SUBJECT(subID) COVTYPE(VC).
```

Appendix 3. *SPSS syntax for linear mixed model results.*