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Changes in Glycemic Load Are Positively Associated with Small Changes in Primary Stress Markers of Allostatic Load in Puerto Rican Women

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ABSTRACT

Background: Puerto Ricans experience a high prevalence of type 2 diabetes. Dietary glycemic load (GL) and allostatic load (AL) have been linked with diabetes. AL, the wear and tear on the body from chronic stress, starts with secretion of primary stress markers from activation of the hypothalamic-pituitary-adrenal (HPA) axis, sympathetic nervous system (SNS), and immune system. GL can act as a physiological stressor, contributing to the primary AL response.

Objective: We examined the relation between GL and a composite score of primary stress markers of AL in Puerto Rican adults.

Methods: Data were from the Boston Puerto Rican Health Study, a cohort study of Puerto Ricans, aged 45–75 y, including 262 men and 697 women with complete data at baseline and 2-y follow-up. GL was calculated from dietary intake obtained with an FFQ. Sex-specific composite primary AL scores included markers of the HPA axis (cortisol and dehydroepiandrosterone sulfate), SNS (epinephrine and norepinephrine), and immune system (C-reactive protein). Linear regression models were stratified by sex and adjusted for covariates.

Results: Mean ± SD baseline GL score was 155 ± 28 for men and 135 ± 34 for women. Mean primary stress AL score was 1.25 ± 1.14 for men and 1.25 ± 1.06 for women. GL was not associated with AL score in men. In women, increasing GL from baseline to 2 y was significantly associated with increasing AL, after adjusting for sociodemographics, physical activity, smoking, BMI, menopause, and baseline AL score ($\beta = 0.03$; $P = 0.049$). Results became marginally significant after further adjustment for chronic diseases ($P = 0.06$) and intake of fats (P values: saturated fats = 0.08; *trans* fats = 0.06; unsaturated fats = 0.07), but the magnitude of the association remained unchanged.

Conclusions: Increasing GL over 2 y was positively associated with increasing composite score of primary markers of AL in Puerto Rican women. More studies are needed to confirm our findings. *J Nutr* 2020;150:554–559.

Keywords: allostatic load, diabetes, glycemic load, Puerto Rican, women

Introduction

Glycemic load (GL), a measure of low carbohydrate quality (i.e., refined carbohydrates), has been linked to increased risk of type 2 diabetes (referred to as diabetes from here on) (1–5). However, 1 meta-analysis reported sex differences, with GL associated with higher diabetes risk among women, but not men (6). Puerto Ricans experience a great burden of diabetes (7) and have a diet characterized by foods high in GL (i.e., rice and starchy vegetables) (8). Because of this, it is particularly important to understand associations between GL and risk factors for diabetes in Puerto Ricans.

The allostatic load (AL) model posits that unhealthy dietary intake acts as a physiological stressor in the body (9). AL is defined as the wear and tear of the body's regulatory systems due to chronic exposure to stress (10, 11), leading to chronic health conditions such as diabetes (10, 11). The concept of AL describes a cause-effect chain triggered by exposure to stress and followed by the secretion of primary stress markers from the hypothalamic-pituitary-adrenal (HPA) axis, cortisol, and dehydroepiandrosterone sulfate (DHEAS), the sympathetic nervous system (SNS; epinephrine and norepinephrine), and the immune system [C-reactive protein (CRP)] (10, 11).

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The accumulation of primary stress markers leads to the development of secondary stress markers, including central adiposity, hypertension, hyperlipidemia, and hyperglycemia (10, 11). In turn, the accumulation of secondary stress markers leads to chronic disease. Although AL is conceptualized as a cascade of events, it is often studied as a composite measure, combining primary, secondary, and tertiary markers into a single score. However, the sequence of responses and their contribution to disease development, as well as the role of sex in this biological process, have not been well studied.

Similarly, few studies have examined the hypothesis that GL acts as a physiological stressor in the body. Previous studies, mostly cross-sectional (12–15), found that a sweets dietary pattern (high in GL) was positively associated with urinary cortisol (12); a dietary pattern high in French fries (high in GL) was negatively associated with DHEAS (13); carbohydrate-rich meals were associated with higher postprandial norepinephrine (16); and GL was positively associated with CRP (14, 15). However, the few longitudinal studies to date on GL and CRP have shown mixed results (17, 18). Methodological differences in study design and measurement of carbohydrate preclude firm conclusions. Refined carbohydrate intake might play a role in the initiation of AL in Puerto Ricans because of the cultural preference for foods high in GL (8), thus contributing to the metabolic disparities observed in Puerto Ricans. The present study aimed to examine the relation between GL and a composite score of primary stress markers of AL in Puerto Rican men and women at baseline and at 2-y follow-up.

Methods

Study participants

The current analysis used data from the Boston Puerto Rican Health Study (BPRHS), described elsewhere (19). Briefly, between 2004 and 2009 the BPRHS enrolled Puerto Rican men and women, aged 45–75 y and residing in the Greater Boston area, using primarily door-to-door enumeration (in census blocks with at least 25 Hispanic adults), but also community events, referrals from recruited individuals, and flyers distributed in the community. Individuals were eligible if they self-identified as Puerto Rican, lived in the Boston metropolitan area, did not have severe cognitive impairment (Mini-Mental State Examination score <10), and planned to stay in the area for ≥2 y. A total of 2093 individuals were identified, of which 1802 were eligible to participate. Informed consent was obtained prior to conducting baseline interviews. Trained bilingual research staff conducted study interviews. This study was approved by the Institutional Review Boards of Tufts University and Northeastern University.

The BPRHS collected information on sociodemographic, behavioral, dietary (through an adapted FFQ), anthropometric (measured during interviews), and biochemical characteristics (12-h urine and fasting blood samples) measured at baseline and 2 y after baseline. Of the 1802 individuals who met study eligibility criteria at baseline, 1500 (83%) agreed to participate and completed interviews [n = 1056 (70.4%) women at baseline]. Of the 1500 enrolled participants, 81% (n = 344 men and 877 women) completed the 2-y follow-up assessment. The current analysis includes data obtained from men and women at both time points. For the present analysis, individuals were ineligible if they had implausible dietary intake at either time point (n = 23 for ≤600 kcal/d; n = 56 for ≥4800 kcal/d). We further excluded participants with missing data for any of the primary markers of AL at baseline or 2-y follow-up (n = 166) or on confounders (n = 17). The final sample included 262 men and 697 women.

Glycemic load

GL was calculated from dietary intake, measured with a 126-item semiquantitative FFQ adapted for Puerto Ricans and previously described elsewhere (20). Briefly, using the National Cancer Institute/Block FFQ as base, food items reported in 24-h recalls by Puerto Rican participants of the Hispanic Health and Nutrition Examination Survey were added. Further, to confirm completeness of the food list, 24-h recalls were conducted among Hispanics residing in Massachusetts (50% Puerto Rican). This FFQ was then validated against 24-h recalls [Pearson correlation for carbohydrate (grams) = 0.84] and several plasma micronutrients (21–23). Using the previous year as the reference period, this questionnaire included foods typically consumed by Puerto Ricans and portion sizes adjusted to the Puerto Rican diet. Nutrient intakes were calculated using the Nutrition Data System for Research software (version 2007; University of Minnesota Nutrition Coordinating Center). GL was calculated as in previous studies (24). Briefly, the International Tables of Glycemic Index (GI) and GL values, with glucose as the reference value, were used. Foods with ≥5 g total carbohydrate/medium portion size were assigned a GI value, whereas those with ≤5 g total carbohydrate/medium portion size were assigned a GI of zero. To select the most appropriate GI value, data on food preparation collected in the FFQ were used. If a specific food had more than 1 GI value, we used the mean value of all available GIs. For foods without published GI values, the value from the most similar food was used. For example, specific Puerto Rican breads without a value would be given the value for white bread. To calculate the GL of a food, the GI was multiplied by grams of available carbohydrate in 1 serving of the food. Lastly, the total dietary GL was calculated by summing the GL scores of all food sources. The total GL values were adjusted for energy intake using the residual method (25), separately for men and women. For the baseline analysis, GL was used as a continuous variable. We further calculated the difference in GL values between time points (GL at year 2 − GL at baseline; positive values indicate an increase in GL and negative values a decrease) to evaluate change in GL and change in primary markers of AL. The difference calculated was also used as a continuous variable in the analysis.

Primary markers of AL

A composite score of the primary markers of AL was used as the dependent variable. Biomarker measures included cortisol, epinephrine and norepinephrine (each from 12-h urine), and DHEAS and CRP (both from fasting blood), representing the HPA axis (cortisol and DHEAS), the SNS (epinephrine and norepinephrine), and inflammation (CRP) (10, 11). Because there are no clinical cutoff scores for most of these measures and given sex differences in AL (26), population- and sex-specific quartiles defined by baseline values of each biomarker were created as in our previous work (27). For each biomarker, an individual received a score of 0 if they were below the sex-specific 75th percentile, or a score of 1 if they had values at or above the sex-specific 75th percentile. This was the opposite for DHEAS. DHEAS is an HPA axis antagonist, with lower concentrations representing dysregulation. Thus, values at or below the sex-specific 25th percentile were assigned a score of 1 and those above the sex-specific 25th percentile a score of 0. A sex-specific summary score for the AL primary markers was then created by summing the scores for each biomarker. The summary score ranged from 0 to 5. AL was used as a continuous variable for the baseline analysis. We then calculated the difference in AL values

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Abbreviations used: AL, allostatic load; BPRHS, Boston Puerto Rican Health Study; CRP, C-reactive protein; DHEAS, dehydroepiandrosterone sulfate; GI, glycemic index; GL, glycemic load; HPA, hypothalamic-pituitary-adrenal; SNS, sympathetic nervous system.

TABLE 1 Baseline characteristics of participants in the Boston Puerto Rican Health Study[1]

	Men				Women			
	Total ($n = 262$) (27.3%)	Bottom GL quartile ($n = 66$)	Top GL quartile ($n = 65$)	*P* value	Total ($n = 697$) (72.7%)	Bottom GL quartile ($n = 175$)	Top GL quartile ($n = 174$)	*P* value
Demographics								
Age, y	56.8 ± 8.2	56.6 ± 7.4	57.8 ± 8.9	0.38	57.2 ± 7.4	56.6 ± 7.3	57.2 ± 6.8	0.42
Education below high school	166 (63.4)	39 (59.1)	41 (63.1)	0.64	455 (65.3)	114 (65.1)	118 (67.8)	0.60
Weight status								
BMI, kg/m^2	29.8 ± 5.0	30.4 ± 5.1	29.3 ± 4.3	0.18	32.9 ± 6.9	33.5 ± 7.3	32.4 ± 6.8	0.16
Experiencing menopause	—	—	—	—	576 (82.6)	140 (80.0)	152 (87.4)	0.06
Behavioral factors								
Smoker				0.80				0.77
Never	80 (30.5)	20 (30.3)	22 (33.9)		359 (51.5)	87 (49.7)	93 (53.5)	
Former	97 (37.0)	25 (37.9)	21 (32.2)		190 (27.3)	48 (27.4)	43 (24.7)	
Current	85 (32.4)	21 (31.8)	22 (33.9)		148 (21.2)	40 (22.9)	38 (21.8)	
Physical activity score	32.7 ± 5.9	33.9 ± 6.8	31.9 ± 5.4	0.07	31.1 ± 4.0	31.1 ± 3.6	31.1 ± 3.9	0.98
Energy from protein, %	16.8 ± 3.0	18.9 ± 3.6	14.7 ± 1.9	<0.01	17.1 ± 3.3	19.8 ± 3.0	14.4 ± 2.1	<0.01
Energy from saturated fats, %	9.8 ± 2.5	11.6 ± 2.9	8.4 ± 1.8	<0.01	9.4 ± 2.3	11.2 ± 2.2	7.9 ± 1.9	<0.01
Energy from polyunsaturated fats, %	8.8 ± 2.1	9.7 ± 2.5	8.0 ± 1.7	<0.01	8.7 ± 2.1	9.5 ± 2.2	7.7 ± 1.8	<0.01
Energy from *trans* fats, %	1.1 ± 0.4	1.2 ± 0.4	1.1 ± 0.4	0.18	1.1 ± 0.4	1.2 ± 0.3	1.0 ± 0.5	<0.01
Prevalence of chronic conditions								
Diabetes	101 (38.7)	27 (40.9)	21 (32.3)	0.31	259 (37.2)	71 (40.6)	54 (31.2)	0.07
Hypertension	140 (70.8)	50 (76.9)	41 (64.1)	0.11	464 (67.0)	121 (69.5)	105 (60.7)	0.08
Hyperlipidemia	205 (78.2)	50 (75.8)	56 (86.2)	0.13	414 (59.4)	99 (56.6)	106 (61.3)	0.37

[1]Values are mean ± SD for continuous variables, or frequency (percentage) for categorical ones. GL, glycemic load.

between time points (AL at year 2 − AL at baseline; with positive values indicating an increase in AL and negative values a decrease) to evaluate change in AL. The difference calculated was also used as a continuous variable in the analysis.

Covariates

Covariates were determined a priori from the literature and included age, education, smoking, physical activity, menopause status in women, and BMI. Sensitivity analyses included additional adjustment for chronic conditions (diabetes, hypertension, and hyperlipidemia), and dietary intake (percentage of energy from protein, saturated fat, *trans* fat, and polyunsaturated fat) all assessed at baseline interviews. Education was measured with the question, "What is the highest grade you completed in school?" and categorized as "below high school" and "high-school graduate or above". Smoking was categorized as current, former, or never smoker. Physical activity was measured with a modified version of the Paffenbarger questionnaire from the Harvard Alumni Activity Survey (28, 29); the calculated score was used as a continuous variable. Women reported their menopause status by answering the question, "Have you already gone through or are you currently going through menopause?" (yes/no). Individuals with chronic diseases (diabetes, hypertension, and hyperlipidemia) were identified through use of medications for each condition or plasma measures of glucose (fasting glucose >125 mg/dL), lipids (HDL <40 mg/dL or total cholesterol >239 mg/dL), and high blood pressure (systolic >139 mmHg; diastolic >89 mmHg). Lastly, BMI (kg/m^2) was calculated from height and weight measures taken by trained study staff.

Statistical analysis

All analyses were, a priori, stratified by sex. Descriptive statistics at baseline included frequencies for categorical variables and mean and SD for continuous variables. Student *t* tests and chi-square tests were used to contrast baseline characteristics by bottom and top quartiles of baseline GL. Multivariable linear regression analyses by sex were used to evaluate the association between GL and primary markers of AL at baseline, and to evaluate the association between change in GL and change in primary markers of AL between baseline and 2 y (both unadjusted and adjusted for baseline primary markers of AL). For each analysis we conducted an unadjusted model (model 1) and a series of adjusted models: model 2 = age and BMI (and menopause status for model in women); and model 3 = model 2 + education + smoking + physical activity. Additional sensitivity analyses included model 3 + chronic diseases; and model 3 + each diet variable separately. Significance was set at $P < 0.05$. STATA version 14 (StataCorp LLC) was used for all analyses.

Results

Baseline characteristics in the total sample and by quartile of GL are shown in **Table 1**. Overall, the sample was 70% female, had a mean age of 57 ± 8 y, and >60% had below high-school education. Most were overweight or obese, with sedentary or lightly active lifestyles. The majority of women were in menopause. Half of the women and one-third of men were never smokers. More than one-third of the sample had diabetes, and ~70% had hypertension. In addition, 80% of men and 60% of women had hyperlipidemia. Demographic characteristics, smoking, and disease status were not significantly different by baseline GL. The mean GL score at baseline was 155 ± 28 for men and 135 ± 34 for women, and it decreased by on average 16.1 ± 30.1 points for men and 17.6 ± 26.1 points for women from baseline to year 2. The mean composite score of primary stress markers of AL was 1.25 ± 1.14 for men and 1.25 ± 1.06 for women, and it increased to 1.46 among men and 1.48 among women by year 2.

GL was not significantly associated with primary stress markers of AL at baseline (**Tables 2** and **3**). In men, change in GL from baseline to 2 y was not associated with change in the composite score of primary stress markers (Table 2). In women, greater change in GL scores from baseline to 2 y was significantly associated with greater change in the composite score of primary stress markers in models adjusted

TABLE 2 Baseline and longitudinal association between GL and primary stress markers of AL among men in the Boston Puerto Rican Health Study[1]

	Outcome: baseline primary markers of AL		Outcome: change in primary markers of AL			
	Baseline GL		GL change		GL change adjusted for baseline AL	
Exposure	β (95% CI)	*P*	β (95% CI)	*P*	β (95% CI)	*P*
Model 1	−0.009 (−0.06, 0.04)	0.71	−0.005 (−0.06, 0.05)	0.85	0.001 (−0.04, 0.04)	0.96
Model 2	−0.006 (−0.06, 0.04)	0.81	−0.007 (−0.06, 0.05)	0.80	0.002 (−0.04, 0.05)	0.94
Model 3	−0.006 (−0.07, 0.04)	0.83	−0.009 (−0.06, 0.04)	0.72	−0.002 (−0.04, 0.04)	0.94

[1] Glycemic load and glycemic load difference are shown in increments of 10 units. Model 1 = unadjusted. Model 2 = age and BMI. Model 3 = model 2 + education + smoking + physical activity. AL, allostatic load; GL, glycemic load.

for age, BMI, and menopause status (Table 3). This association became marginally significant in models further adjusted for behavioral factors (model 3, $P = 0.056$), but coefficients remained similar. Results also remained similar after further adjustment for baseline composite score of primary stress markers. In sensitivity analyses, further adjustment for chronic diseases and diet variables did not change the magnitude of the coefficients, but results were marginally significant (*P* adjusted for chronic disease = 0.06; *P* adjusted for saturated fats = 0.08; *P* adjusted for *trans* fats = 0.06; *P* adjusted for unsaturated fats = 0.07). Lastly, we evaluated GI as another measure of carbohydrate nutrition and, although estimates were similar to those of GL, none of the models were statistically significant (data not shown).

Discussion

To our knowledge, this is the first study to evaluate the association between GL and a composite score of primary stress markers of AL. We found that neither GL at baseline nor change in GL were significantly associated with the composite score of primary stress markers of AL in men. Findings in women showed that greater change in GL from baseline to 2 y was significantly associated with small changes in the composite score of primary stress markers of AL. However, in sensitivity analyses, this association became marginally significant with further adjustment for chronic diseases and other diet variables. This might be expected, because individuals with high dietary GL have lower consumption of other macronutrients and these intakes cannot be clearly separated. The finding of GL change being associated with changes in primary AL markers is consistent with associations between other measures of carbohydrate consumption and individual primary stress markers of AL observed in several cross-sectional studies (12–15). An analysis with baseline BPRHS data previously showed that a sweets dietary pattern (defined by foods high in GL) was positively associated with urinary cortisol (12). Another baseline BPRHS analysis showed that a dietary pattern characterized by high intake of French fries (high in GL) was negatively associated with the HPA axis antagonist DHEAS (13). In addition, 2 cross-sectional studies using data from the Women's Health Study showed positive associations between GL and CRP (14, 15). Lastly, an experimental study that supplied a carbohydrate-rich meal showed that norepinephrine increased following the carbohydrate-rich meal (16). Thus, some of our findings among women are in line with these studies.

Few other studies have evaluated the association between GL and a composite score of AL (including primary and secondary markers). One study, conducted with Japanese women, found that intake of vegetables (a food group low in GL) was associated with low AL (30). In addition, cross-sectional data from BPRHS men and women showed that a dietary pattern characterized by intake of French fries (a food high in GL) was associated with higher AL (13). Thus, although these studies do not directly evaluate GL and included other secondary markers of AL, they provide indirect support for our findings.

The majority of the available studies are cross-sectional and provide some evidence of GL being associated with primary markers of AL (12–15, 30). However, our cross-sectional analysis with baseline data did not show that GL was significantly associated with the primary stress markers of AL. This discrepancy might be due to the different ways in which intake of refined carbohydrate is measured (GL compared with dietary patterns compared with specific foods high in carbohydrates), or to the different outcomes evaluated (composite score of only primary markers compared with each primary marker individually compared with composite score of all AL markers). Additionally, the lack of association between GL and the composite score of primary markers of AL at baseline could be due to the fact that many of those participants with diabetes, who are also likely to have higher primary markers of AL, had already made dietary changes (due to their diabetes diagnosis) to decrease sugar intake and therefore GL. It is possible that exposure to increased GL influences the observed

TABLE 3 Baseline and longitudinal association between GL and primary stress markers of AL among women in the Boston Puerto Rican Health Study[1]

	Outcome: baseline primary markers of AL		Outcome: change in primary markers of AL			
	Baseline GL		GL change		GL change adjusted for baseline AL	
Exposure	β (95% CI)	*P*	β (95% CI)	*P*	β (95% CI)	*P*
Model 1	−0.01 (−0.05, 0.02)	0.41	0.03 (0.0001, 0.07)	0.049	0.03 (0.003, 0.06)	0.029
Model 2	−0.01 (−0.05, 0.02)	0.41	0.03 (0.0001, 0.07)	0.049	0.03 (0.0007, 0.06)	0.045
Model 3	−0.01 (−0.04, 0.02)	0.46	0.03 (−0.0009, 0.07)	0.056	0.03 (0.0001, 0.06)	0.049

[1] Glycemic load and glycemic load difference are shown in increments of 10 units. Model 1 = unadjusted. Model 2 = age + BMI + menopause. Model 3 = model 2 + education + smoking + physical activity. AL, allostatic load; GL, glycemic load.

change in primary AL markers. Due to this discrepancy and the lack of longitudinal analyses in the literature evaluating GL and the primary AL response, longitudinal studies are needed to truly understand this relation.

In our sample, GL was not associated with the composite score of primary stress markers of AL in men. Our sample size for men was smaller than that for women, which might account, in part, for nonsignificant results. It is also possible that GL is not associated with primary markers of AL in men. As previously mentioned, sex differences in the association between GL and risk of diabetes have been reported (6), where, consistent with our findings, it was only significant for women. Although some studies suggest that sex differences in carbohydrate and glucose metabolism exist (31, 32), more studies are needed to comprehend how GL might differentially affect glucose metabolism and primary AL markers in men and women.

Our findings fill important research gaps in that they are based on data that allow us to evaluate changes in the exposure and outcome, and to incorporate a comprehensive set of biomarkers to capture the primary AL response. Most of the previous studies examining associations between refined carbohydrates and primary stress markers examined individual markers and used a cross-sectional design (12–15, 30). With data available for 2 time points, our study was able to consider change in GL over 2 y with change in primary markers of AL over the same time period. Previous studies do not fully evaluate the primary AL response, but evaluate primary markers individually (12–15) or incorporate the primary markers along with the secondary markers (13, 30). Our study incorporated a composite score of primary markers of AL that represent the systems that are first activated in the AL response: the HPA axis, SNS, and the immune system.

Overall, our findings that an increase in GL is associated with an increase in a composite score of primary markers of AL in models adjusted for biological (age, menopause, and BMI) and behavioral/sociodemographic factors (physical activity, education, and smoking) suggest that GL could be a physiological stressor for women that contributes to dysregulation and activation of the primary AL response. Animal studies provide evidence that carbohydrates can stimulate the SNS and thus increase release of some primary markers of AL (33, 34). Because some of these markers are known to increase blood glucose concentration (35, 36), and are hypothesized to trigger secondary markers of AL (9, 10), which include markers of glucose metabolism, understanding the relation between GL and primary markers of AL could help in understanding how high GL influences glucose metabolism and diabetes. This is of great importance to Puerto Ricans, given their high intake of foods high in GL (i.e., white rice, sugary drinks, and starchy vegetables) and their high prevalence of diabetes. It is important to note that although our findings remained similar in magnitude, they became marginally significant when further adjusted for intakes of protein and fat. Thus, it is possible that protein and fat intakes also play an important role in initiation of the AL response. Because these each contribute to total energy intake, an increase in one is inextricably linked to decreases in the others. However, this does not negate the observation that a total pattern high in GL and lower in other energy nutrients was associated with AL. Thus, more longitudinal studies are needed to confirm our findings and to evaluate the role of other diet variables.

The study results should be considered with certain limitations and strengths in mind. One limitation is that GL was measured with an FFQ and calculated from self-reported data that are susceptible to bias. However, the FFQ used in this study was specifically adapted for this population by including ethnically appropriate foods and recipes, and has been validated against 24-h dietary recalls in Latinos (20). It is important to mention that a portion of participants were excluded due to missing data (16% in women and 15% in men). However, missingness was mainly due to primary markers of AL (90% of missing cases in women and 94% in men). Excluded women due to missing data were similar to included women in all covariates, but they had slightly lower baseline GL and subsequently lower changes in GL (8-unit difference). Similarly, excluded men due to missing data were similar to included men in all covariates and in baseline GL, but they had greater changes in GL (25-unit difference). Another limitation is that the study included only Puerto Ricans, which could limit generalizability to other Latino groups. However, the focus of Puerto Ricans is also a strength, because Puerto Ricans comprise the largest Latino group in the northeastern United States (37), and experience considerable disparities in diabetes (38), but have been underrepresented in research. In addition, a strength of our analysis is the use of a composite measure of primary stress markers of AL to understand the initial AL response, and the availability of longitudinal data that allowed us to explore changes in GL and changes in primary markers of AL.

In conclusion, an increase in GL over 2 y was associated with small increases in a composite score of primary markers of AL in women. Studies with larger samples of men are needed to understand this relation in men. In addition, more longitudinal studies are needed to understand the relation between GL and the primary AL response and to test interventions that improve GL in Puerto Rican women.

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