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Association between a Healthy Lifestyle Score and inflammatory markers among Puerto Rican adults

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Abstract *Background and aims:* The relationship between multiple lifestyle components analyzed in combination and inflammation remains understudied. We aimed to assess the association between a Healthy Lifestyle Score (HLS) that includes adherence to five behavioral components (diet, physical activity and sedentary behaviors, smoking, social support and network, and sleep) and inflammatory markers, as well as the role of the HLS in inflammation among individuals with cardiometabolic conditions, in Puerto Rican adults.

Methods and results: In a cross-sectional study of 842 Puerto Ricans adults (aged 45–75 y) living in Boston, MA, the HLS (range = 0–190; maximum indicative of healthiest adherence) was analyzed for association with three inflammatory markers: interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), and C-reactive protein (CRP). In multivariable-adjusted models, the HLS was inversely associated with IL-6 ($\beta \pm SE = -0.55 \pm 0.13$; $P < 0.001$) and TNF-α (-0.39 ± 0.13; $P = 0.004$). The dietary and smoking components were associated with both inflammatory markers independently of the other HLS components. Significant inverse associations were observed for each 20-unit increase in HLS and IL-6 and TNF-α for participants with hypertension (n = 600; $\beta \pm SE = -0.58 \pm 0.16$; -0.46 ± 0.16, respectively) and with overweight/obesity (n = 743; $\beta \pm SE = -0.59 \pm 0.13$; -0.50 ± 0.14, respectively), but not for those with diabetes (n = 187) or heart disease (n = 192). The HLS was not associated with CRP, after adjustment for potential confounders.

Conclusion: Higher adherence to multiple lifestyle behaviors was associated with lower concentrations of inflammatory markers. Because low-grade inflammation may precede chronic diseases, following an overall healthy lifestyle may help lower risk of these diseases.

Introduction

Scientific evidence suggests that chronic low-grade inflammation may play a role in the pathology of cardiometabolic diseases [1–3]. For instance, higher concentrations of inflammatory markers such as interleukin-6 (IL-6), tumor necrosis factor (TNF-α), and C-reactive protein (CRP) have been shown to be associated with higher

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cardiovascular risk [3,4]. In addition, lifestyle behaviors may underlie the inflammatory processes, as posited by several studies reporting an inverse association between inflammatory markers and adherence to overall dietary patterns [5–9] or physical activity [10–12]. Other lifestyle behaviors, such as smoking [13] or sleep [14], have also been linked to inflammatory response. Additionally, emerging research suggests that social support and network may have a role in mediating the psychological impact of life stressors, which may trigger inflammation [15,16].

Despite the evidence suggesting that inflammation resulting from individual lifestyle habits may underlie pathophysiological processes, the role of multiple lifestyle components analyzed together as a single score on inflammatory markers, and its potential mediation in the presence of chronic conditions, remains understudied. We recently developed and validated a Healthy Lifestyle Score (HLS), which includes a combination of multiple behaviors (diet, physical activity and sedentary behaviors, smoking, social support and network, and sleep), and showed that adhering to an overall healthy lifestyle may provide stronger protection against cardiometabolic and neuroendocrine factors than individual lifestyle components, in Puerto Rican adults [17]. We reported previously that this population had high prevalence of multiple chronic conditions [18], and we hypothesize that Puerto Ricans, especially those with prevalent chronic conditions, may have lower inflammatory markers by adhering to an overall healthy lifestyle. We have shown that the lifestyle behaviors of the HLS are correlated, thus combining established and emerging risk behaviors into one single measure of whole lifestyle may be more useful in assessing associations with inflammation outcomes than single behaviors. Strategies targeting various lifestyle behaviors together may have higher public health impact. Therefore, we aimed to assess the association between the HLS and inflammatory markers among Puerto Rican adults, as well as participants with cardiometabolic conditions.

Methods

Study population

The design and procedures of the Boston Puerto Rican Health Study (BPRHS), an ongoing longitudinal cohort study, were described in detail previously [18]. Briefly, eligible participants were of self-reported Puerto Rican descent, aged 45–75 y, living in the Boston, MA area, and able to answer interview questions in English or Spanish. Participants for the present analysis were part of an ancillary study immediately following the 2-year follow-up, when data on inflammatory markers (not collected at baseline) as well as lifestyle and sleep habits were collected. Baseline recruitment of 1500 participants was conducted in 2004–2009, and 2-year follow-up was completed by 1276 participants in 2007–2011. The ancillary study was completed by 974 participants. These studies were approved by the Institutional Review Boards at Tufts Medical Center, Tufts University, and Northeastern University. Informed consent was obtained from all participants.

Lifestyle behaviors

Dietary intake was assessed using a semiquantitative food frequency questionnaire specifically developed and validated for this population [19]. Reported food intakes were converted into gram amounts and food groups were created. Disaggregated intake from mixed dishes was added to the appropriate food group. Nutrient intakes were calculated from the Nutrition Data System for Research software (Nutrition Coordinating Center, Minneapolis). Participants reporting implausible energy intakes ($\leq$2510 or $\geq$20 083 kJ/d) or with $\geq$10 questions left blank were excluded (n = 16).

Smoking information was collected with a comprehensive questionnaire asking about type and frequency of use of tobacco products. Smoking was categorized as never ($<$100 cigarettes in entire life, n = 390), former (smoked in the past, but not currently, n = 282), or current smoker (n = 170). A physical activity score was defined by multiplying the self-reported hours spent in heavy, moderate, light, or sedentary activities in 24 h by weighing factors that parallel the rate of oxygen consumption associated with each activity [20]. Information about social support and network was collected with the Norbeck Social Support Questionnaire [21]. Social activities were assessed by the Social and Community Support and Assistance Questionnaire [22]. Sleeping pattern questions included indicators of sleep quantity (total hours of sleep in a 24 h period) and sleep quality [23].

Healthy Lifestyle Score

The development, rationale, and scoring criteria of the HSL and each lifestyle component have been previously described in detail [17]. Briefly, the score included five lifestyle behavioral components selected based on current population-wide recommendations and evidence of association with chronic disease: 1) diet, 2) physical activity and sedentary behaviors, 3) smoking, 4) social support and network, and 5) sleep quality and quantity. The diet quality component was defined following American Heart Association (AHA) recommendations for CVD risk reduction for the general population, using a score previously developed and validated in this population [17]. The AHA diet score ranged from 0 to 90 and included fruit and vegetables, whole grains, fish, dietary fats and cholesterol, added sugars, sodium, and alcohol. For physical activity and sedentary behavior (0–30 points), we included 0–20 points for sedentary (0 points), light (10–20 prorated linearly), or moderate/vigorous activity (20 points), and 0–10 points for hours spent watching television as a measure of sedentary behaviors (prorated linearly). For smoking (0–30 points), we categorized current smokers (0 points), former smokers (10 points), and never smokers (30 points). The social support and network component (0–20

points) was defined by 4 subcomponents of 5-points each: 1) size of social network; 2) average of emotional support from social network; 3) average assistance from social network; and 4) number of social activities. For this analysis, all measures corresponded to the timeline of data collection of the inflammation outcomes, except for the social activities subcomponent, which was measured at baseline, but not collected at the 2-year follow-up. We would expect minimal changes in this sub-component within that period, as suggested by the similar mean scores for the social component without social activities at baseline and 2-year (mean (SD): 7.5 (4.0) vs. 7.9 (3.7), respectively). Finally, for sleep (0–20 points), we considered both quantity (0–10 points, highest for 8 h of sleep) and quality (0–10 points) of sleeping behaviors. The total HLS ranged from 0 to 190 points, with higher score reflecting better adherence to lifestyle recommendations.

Outcome measures

Blood samples for the analysis of TNF-α, IL-6 and CRP were drawn during the ancillary study by trained phlebotomists at the USDA Human Nutrition Research Center on Aging at Tufts University, after an overnight fast. Serum TNF-α and IL-6 concentrations were measured by non-cross-reacting enzyme-linked immunoassays (ELISAs) employing specific monoclonal and polyclonal antibodies for the analysis of specific cytokine antigens (Quantikine ELISA, R&D Systems, Minneapolis, MN, USA). The lower detection limit of the ELISA was reported by the manufacturer to be 4.4 for TNF-α and 0.094 pg/mL for IL-6. Plasma CRP was measured by Immulite 1000 High Sensitive CRP Kit (LKCRP1) on the Immulite 1000 (Siemens Medical Solutions Diagnostics, Los Angeles, CA). The intra- and inter-assay CVs (%) for these analyses were 1.6% and 3.3% for IL-6, 5.3% and 10.8% for TNF-α, and 5.2% and 7.3% for CRP.

Covariates

A sociodemographic questionnaire was used to collect data on age, sex, educational attainment (<8th grade, 9th–12th grade, some college or higher), and household income. Validated questionnaires were used to assess perceptions of one's life as stressful (Perceived Stress Scale), depressive symptomatology (Center for Epidemiologic Studies Depression Scale (CES-D) 20-item scale), and functional limitation of activities of daily living (12-item Activities of Daily Living Score (ADLS)), as described previously [18]. BMI was calculated as weight (kg) divided by height (m) squared. White blood count was assessed from whole blood using electronic impedance, light scatter reaction with a HORIBA ABX Pentra 60C+ analyzer. Manifestation of disease was defined as previously detailed [18]: fasting blood glucose ≥126 mg/dL or medication use for diabetes; systolic/diastolic blood pressure ≥140/90 mmHg or medication use for hypertension; self-reported medical diagnosis for heart disease (heart attack, heart disease or stroke), and BMI ≥ 25 kg/m^2 for overweight/obesity.

Statistical analysis

Of the 1276 participants with 2-year data, we had complete HLS information for 842 participants. To maximize statistical power, we included the largest sample size with available information for each HLS component and each inflammatory biomarker when these were analyzed individually: 1181 for diet; 1223 for physical activity and sedentary behavior; 1226 for smoking; 849 for social network; and 927 for sleep.

The HLS was used as a continuous measure and was also divided into tertile categories. IL-6, TNF-α, and CRP variables were log-transformed to normalize data distributions. We calculated baseline characteristics across tertiles of the HLS by using analysis of variance for continuous variables and chi-square analyses for categorical variables. Linear regression models were used to obtain adjusted means for age, sex, and total energy intake. Linear *P*-trend was tested across tertiles of HLS distribution. General linear models were used to determine associations between each 20-unit increase in the overall HLS, and 5-unit increase of the separate five components of the HLS as continuous exposure, and each inflammatory marker as outcome, adjusting for potential confounders. Models were fitted as follows: Model 1 = age, sex, energy intake, educational attainment, household income; Model 2 = Model 1+ perceived stress, depressive symptomatology, ADL, BMI, and white blood cell count (to control for elevation in inflammatory markers from acute infections). When testing each component of the HLS separately, we further adjusted each model for the other lifestyle components. Similar models for participants presenting cardiometabolic conditions (type 2 diabetes, hypertension, heart disease, and overweight/obesity) were run. We tested for effect modification with such conditions by including a cross-product term in the regression model. Results for linear regression models are reported as beta-coefficient (β) and SE.

Statistical analyses were conducted using SAS version 9.4 (SAS Institute). A significance level of $P < 0.05$ was used.

Results

The HLS was normally distributed and the mean (SD) was 73.7 (20.4). Those in the highest HLS tertile were more likely to be older, women, and to have higher total household income and educational attainment (Table 1). They were also more likely to report lower perceived stress, depressive symptomatology, and functional limitation, compared to those in the lowest tertile ($P < 0.001$).

Each 20-unit increase in the HLS was inversely associated with IL-6 ($\beta \pm SE = -0.55 \pm 0.13$; $P < 0.001$) and TNF-α (-0.39 ± 0.13; $P = 0.004$) after adjustment for potential confounders (Table 2). The significant inverse association between the HLS (-0.15 ± 0.07; $P = 0.035$), as well as the physical activity component (-0.31 ± 0.08; $P < 0.001$), and CRP, became null after including psychosocial covariates. Analyses with variables as 5-unit increases for each

Table 1 Characteristics of Puerto Rican adults across tertiles of the Healthy Lifestyle Score.[a]

	Healthy Lifestyle Score (n = 842)[a]			
	Tertile 1 (37.4–62.5)	Tertile 2 (65.7–80.7)	Tertile 3 (85.5–110.4)	*P*-trend
n	280	281	281	
Age (y)	58.0 ± 7.6	58.9 ± 7.4	59.4 ± 7.5	0.023
Female (%)	67.9	75.1	77.6	0.025
BMI (kg/m^2)	32.5 ± 7.3	32.6 ± 6.3	32.0 ± 5.9	0.34
Total household income ($/y)	13 604 ± 9251	17 539 ± 17 607	20 879 ± 26 522	<0.0001
Educational attainment (%)				<0.0001
Less than 8th grade	37.5	35.2	14.7	
9–12th grade (or GED)	33.8	32.3	34.9	
Some college or higher	48.2	32.6	50.4	
Perceived stress scale[b]	25.3 ± 8.5	23.5 ± 8.8	20.3 ± 8.4	<0.0001
Depressive symptomatology from CES-D score[c]	21.8 ± 12.8	18.9 ± 12.7	14.6 ± 11.6	<0.0001
Functional limitation in ADL[d]	5.5 ± 6.1	3.4 ± 4.5	2.4 ± 6.6	<0.0001
Healthy Lifestyle Score	51.0 ± 9.4	73.5 ± 5.4	96.5 ± 9.8	<0.0001
Healthy Lifestyle Score components[e]				
Diet score (0–90)[f]	23.6 ± 0.5	28.4 ± 0.5	36.1 ± 0.5	<0.0001
Physical activity and sedentary behavior score[g]	6.9 ± 0.4	10.9 ± 0.4	15.6 ± 0.4	<0.0001
Smoking score (0–30)[g]	7.0 ± 0.5	18.3 ± 0.5	26.5 ± 0.5	<0.0001
Social support score (0–20)[g]	8.8 ± 0.2	10.5 ± 0.2	12.8 ± 0.2	<0.0001
Sleep score (0–20)[g]	8.0 ± 0.3	10.3 ± 0.3	12.1 ± 0.3	<0.0001

BMI, Body Mass Index; GED, General Education Development; ADLS, Activities of daily living Score.
[a] Continuous variables are expressed as mean (standard deviation); categorical variables as percentages. Tertiles are expressed in the 10th and 90th percentiles of the Healthy Lifestyle Score in each category. *P*-trend for linear trend across tertiles of the Healthy Lifestyle Score.
[b] Perceived Stress Scale (score range: 0–56).
[c] CES-D, Center for Epidemiologic Studies Depression Scale (score range: 0–60).
[d] ADLS: Activities of daily living Score (score range: 0–36).
[e] Healthy Lifestyle Score (0–190), Diet score (score range: 0–90), Physical activity and sedentary behavior (score range: 0–30), Smoking score (score range: 0–30), Social support score (score range: 0–20), Sleep score (score range: 0–20). A higher score reflects better adherence.
[f] Age, sex and energy adjusted (mean ± SEM).
[g] Adjusted for sex and age (mean ± SEM).

individual component of the HLS showed that the diet and the smoking components were protectively associated with IL-6 (−0.75 ± 0.24, $P = 0.002$ and −0.85 ± 0.35, $P = 0.01$; respectively) independently from the other lifestyle components. Having a better score in the smoking component was also inversely associated with TNF-α (−1.08 ± 0.35, $P = 0.002$). Physical activity and sedentary behavior, as well as social support, were each significantly associated with IL-6, but were attenuated after adjusting for the other components of the HLS (Table 2). We also assessed the standardized betas in order to compare the weight provided by each component, and these were shown to be stronger for diet and smoking, compared to the other lifestyle components.

Finally, the inverse association between each 20-unit increase in HLS and lower IL-6 and TNF-α remained significant for participants with cardiometabolic conditions, specifically hypertension (−0.58 ± 0.16; −0.46 ± 0.16, respectively) and with overweight/obesity (−0.59 ± 0.13; −0.50 ± 0.14, respectively), but not for diabetes or heart disease (Table 3). No significant effect modification was found (data not shown). The HLS was not associated with CRP for participants with any condition.

Discussion

In this Boston Puerto Rican population we found that adherence to an HLS that comprises multiple lifestyle behaviors was significantly associated with lower inflammatory markers, and this association was stronger than that of its individual components. Our results suggest that strategies to improve a set of healthy lifestyles may be an effective real-life approach to prevent inflammatory dysregulation in at-risk populations, such as Puerto Ricans.

Consistent with previous literature, we observed that those with lower income and educational attainment had lower adherence to the HLS [10,11]. Although having higher socioeconomic and educational status can help support a healthy lifestyle environment, in our analysis the HLS remained significantly associated with inflammatory markers even after adjusting for such factors. Most previous studies on inflammation limited their analyses to individual risk factors, rather than the combined effects of multiple lifestyle behaviors [24–26]. It is thus difficult to compare our HLS results with the existing literature. In our analysis, a 20-unit increase in the HLS was associated with two inflammatory markers, as hypothesized, but not with CRP after adjusting for psychosocial factors and BMI (possible mediators or confounders in the association with inflammation [15]), as well as white blood cell count, which accounts for acute inflammation.

The scores for diet and smoking were independently associated with IL-6, and smoking was associated with TNF-α as well. Consistent with our results, associations between dietary factors and inflammatory markers have been reported by several studies [5,7,8,24–26]. However,

Table 2 Cross-sectional associations for 20-unit increase of the overall Healthy Lifestyle Score and 5-unit increase of each of its components and inflammatory markers in Puerto Rican adults.[a]

	Log IL-6 (pg/ml)		Log TNF-α (pg/ml)		Log CRP (mg/L)	
	β ± SE	P	β ± SE	P	β ± SE	P
Healthy Lifestyle Score (n = 842)						
Model 1[b]	−0.69 ± 0.13	<0.0001	−0.43 ± 0.14	0.002	−0.15 ± 0.07	0.035
Model 2[c]	−0.55 ± 0.13	<0.0001	−0.39 ± 0.13	0.004	−0.06 ± 0.07	0.45
Standardized β[c]	−0.16		−0.10		−0.03	
Diet (n = 1181)						
Model 1[b]	−0.59 ± 0.20	0.0028	−0.06 ± 0.22	0.79	−0.17 ± 0.10	0.08
Model 2[c]	−0.77 ± 0.22	0.0004	−0.07 ± 0.22	0.76	−0.21 ± 0.11	0.054
Model 3[d]	−0.75 ± 0.24	0.0018	−0.02 ± 0.25	0.93	−0.04 ± 0.13	0.74
Standardized β[d]	−0.13		−0.003		−0.01	
Physical activity and sedentary behaviors (n = 1223)						
Model 1[b]	−0.76 ± 0.17	<0.0001	−0.22 ± 0.19	0.25	−0.31 ± 0.08	<0.0001
Model 2[c]	−0.40 ± 0.18	0.031	−0.17 ± 0.19	0.36	−0.15 ± 0.09	0.09
Model 3[d]	−0.23 ± 0.20	0.26	−0.08 ± 0.20	0.70	−0.15 ± 0.11	0.17
Standardized β[d]	−0.02		−0.01		−0.06	
Smoking (n = 1226)						
Model 1[b]	−0.95 ± 0.28	0.0009	−1.16 ± 0.32	0.0003	0.15 ± 0.14	0.30
Model 2[c]	−1.02 ± 0.31	0.001	−1.10 ± 0.31	0.0004	0.10 ± 0.16	0.51
Model 3[d]	−0.85 ± 0.35	0.014	−1.08 ± 0.35	0.002	0.14 ± 0.19	0.48
Standardized β[d]	−0.10		−0.11		0.03	
Social support and network (n = 849)						
Model 1[b]	−0.22 ± 0.11	0.043	−0.18 ± 0.13	0.17	−0.10 ± 0.06	0.13
Model 2[c]	−0.25 ± 0.12	0.044	−0.18 ± 0.13	0.15	−0.08 ± 0.07	0.25
Model 3[d]	−0.19 ± 0.12	0.13	−0.11 ± 0.13	0.37	−0.04 ± 0.07	0.54
Standardized β[d]	−0.06		−0.03		−0.03	
Sleep (n = 927)						
Model 1[b]	−0.14 ± 0.13	0.26	−0.06 ± 0.14	0.67	−0.10 ± 0.07	0.16
Model 2[c]	0.07 ± 0.14	0.62	−0.01 ± 0.14	0.95	0.02 ± 0.08	0.77
Model 3[d]	0.03 ± 0.15	0.85	−0.01 ± 0.15	0.97	−0.03 ± 0.08	0.67
Standardized β[d]	0.01		−0.002		−0.02	

IL-6, Interleukin 6; TNF-α, tumor necrosis factor; CRP, C-reactive protein.
[a] Values are beta-coefficient (β) ± SE.
[b] Model 1: Adjusted for age, sex, energy intake, educational attainment, and household income.
[c] Model 2: Model 1+ white blood cell count, depressive symptomatology, functional limitation in activities of daily living, perceived stress, and BMI.
[d] Model 3: Model 2+ further adjusted for the other components of the HLS.

not all studies have shown association with CRP [27,28], similar to our findings. The difference in constructs used to capture diet may partly explain the inconsistent results. Our finding of the independent association between smoking and IL-6 and TNF-α is substantially supported by the literature [13,24,25]. The lack of the association between smoking and CRP may be due to the sequence of the tobacco cascade operation (smoking increases serum concentration of IL-6 and that leads to raised CRP concentration [26]), or timing of the smoking cessation resulting in a delayed decrease of CRP [25].

We found a protective association between physical activity and sedentary behavior and CRP that was no longer significant when adjusted for psychosocial factors and BMI. The evidence for physical activity and inflammation is inconsistent; while some studies have reported

Table 3 Association between the Healthy Lifestyle Score and inflammatory markers among Puerto Rican adults with cardiometabolic conditions.[a]

	Diabetes (n = 187)	Hypertension (n = 600)	Heart disease (n = 192)	Overweight/obesity (n = 743)
Log IL-6 (pg/ml)	−0.07 ± 0.29	−0.58 ± 0.16*	−0.27 ± 0.32	−0.59 ± 0.13*
Log TNF-α (pg/ml)	0.01 ± 0.33	−0.46 ± 0.16*	−0.49 ± 0.35	−0.50 ± 0.14*
Log CRP (mg/L)	0.12 ± 0.15	0.04 ± 0.09	−0.13 ± 0.17	0.02 ± 0.07

IL-6, Interleukin 6; TNF-α, tumor necrosis factor; CRP, C-reactive protein.
[a] Values are beta-coefficient (β) ± SE for each 20-unit increase in Healthy Lifestyle Index. *P < 0.005 after adjusting for age, sex, energy intake, educational attainment, household income, white blood cell count, depressive symptomatology, functional limitation in activities of daily living, perceived stress, and BMI (except for overweight/obesity). Manifestation of disease was defined as: fasting blood glucose ≥126 mg/dL or medication use for type 2 diabetes; systolic/diastolic blood pressure ≥140/90 mmHg or medication use for hypertension; self-reported medical diagnosis for heart disease (heart attack, heart disease or stroke), and BMI ≥ 25 kg/m^2 for overweight/obesity.

an association with CRP and IL-6 independent of BMI [10,11,29], others found no association or the association was null when adjusted for adiposity markers [24,26,30]. Furthermore, we found that IL-6 was associated individually with physical activity and sedentary behavior, and with social support, but that these associations were attenuated when adjusted for the other components of the HLS, suggesting that they were not independent of the other lifestyles behaviors. Although some studies have found a protective association between social support and inflammation [16], the joint effect with other health behaviors, as suggested by our findings, or its positive link with physiological well-being, may be influencing the inflammatory process. No associations were found for the sleep component, which merits further investigation.

The observation of slightly stronger associations between higher HLS and lower IL-6 and TNF-α among hypertensive and obese participants suggests that after having such conditions, they may benefit from following healthier behaviors to reduce inflammation. Chrysohoou et al. found similar results when studying the adherence to a Mediterranean pattern with inflammatory markers in high CVD risk groups [6]. We did not detect significant associations between HLS and any of the inflammatory markers among those with diabetes or heart disease, likely due to a lack of statistical power due to the relatively low sample size. Because of this, and of the cross-sectional design of the study, results must be interpreted with caution, and we cannot conclude that having diabetes blunts the advantageous effect of a healthy lifestyle on inflammation. On the contrary, other studies suggest that patients with diabetes can benefit from healthy lifestyle behaviors [25,29]. Further research is needed to elucidate these findings. In addition, other inflammatory mediators not analyzed in our study such as IL-1 (key contributor to the pathogenesis of diabetes) could instead be initiating the cytokine network contributing to these conditions [1].

Some limitations of this analysis have to be considered. First, while it is biologically plausible that lifestyle behaviors precede an inflammatory response and subsequent cardiometabolic dysregulation, we cannot determine temporal associations, due to the cross-sectional study design. Second, because lifestyle information was self-reported, measurement error and misclassification may occur. However, we used validated questionnaires for this population to lessen such limitation. Furthermore, we were not able to capture other exposures that may influence the outcomes, such as specific time of smoking cessation or secondhand smoke exposure, for which there is evidence of association with inflammation [25]. Third, the generalizability of the results could be limited by the nature of the population, Puerto Ricans with high prevalence of risk factors. However, the HLS may be applicable to other populations after properly adapting it.

The strengths of this investigation include the study of an overall score comprising several lifestyle components representative of real-life behaviors operating together, which allows for a more complete understanding of their influence on inflammation and cardiometabolic outcomes over isolated components. Thus, the results may be better translated into practical population-wide recommendations. Although the intricacies of the HLS may limit its use in clinical or public health settings, it is an appropriate and valid tool in epidemiological studies of lifestyle behaviors and outcomes related to inflammation and chronic diseases. Subsequent studies should focus on deriving a simple, shorter but validated version of the HLS questionnaire for general use in community or clinical settings. Additionally, the HLS was based on current guidelines and scientific evidence, and despite the different weight of the components, we found consistent associations when using standardized measures. Finally, we adjusted for psychosocial factors that may mediate or confound the associations, as well as for white blood cell count to account for acute infections.

In conclusion, in this Boston Puerto Rican population, higher adherence to multiple lifestyle behaviors was associated with lower concentrations of inflammatory markers in the general population and those presenting chronic conditions. Because low-grade inflammation may precede chronic diseases, following an overall healthy lifestyle may help reduce risk of these diseases. Analyzing the all-inclusive synergistic role of modifiable behavioral contributors to disease may provide a better understanding on how lifestyle choices influence inflammation and cardiometabolic health. Our findings emphasize the need for holistic behavioral approaches as a mean of primary prevention.

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