Longer Leukocyte Telomere Length Predicts Stronger Response to a Workplace Sugar Sweetened Beverage Sales Ban: An Exploratory Study

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ABSTRACT

Background: Shorter leukocyte telomere length (LTL) is associated with increased risk for a number of metabolic diseases including insulin resistance and the development of type 2 diabetes mellitus. Shorter LTL is also associated with stress reactivity suggestive of a possible role for LTL to predict response to behavioral interventions. However, few studies have evaluated how interventions, such as weight loss or dietary changes, are associated with LTL changes or whether LTL can predict behavioral responses to interventions.

Objective: We evaluated metabolic changes in relation to LTL changes and LTL at baseline in a cohort of at-risk adults in response a 10-month workplace-based sugar sweetened beverage (SSB) intervention. Methods: At baseline, metabolic health and LTL measurements were assessed through standard blood draws on 212 participants. Multivariable linear regression
models were used to assess changes in anthropometrics, SSB consumption and 13 blood-based metabolic risk factors, in relation to LTL at baseline and changes in LTL.

**Results:** Longer LTL at baseline was associated with younger age (Beta =-0.49; p<0.01) and female gender (p=0.01). Longer LTL at baseline was also associated with decreases in SSB consumption over the 6-month follow-up period (Beta=-29.67, p=0.04). Slower LTL attrition rates were associated with decreases in waist circumference (Beta = -0.27; p = 0.03) and decreases in HDL-C (Beta = -0.20; p = 0.05), and ApoA1 (Beta = -0.09; p = 0.01).

**Conclusions:** Longer LTL at baseline predicted a favorable overall response to a behavioral intervention -- decreases in SSB consumption. Abdominal adiposity losses paralleled slower declines in LTL suggestive of over health benefits, but we found differences between metabolic changes and LTL at baseline compared with LTL attrition rates. Longer LTL may be a proxy marker of a positive behavioral response.

**Key words:** Telomere, SSB, sugar sweetened beverages, lipids
INTRODUCTION

Telomeres are the caps on the edges of chromosomes that protect the DNA from damage. Telomeres are particularly sensitive to oxidative stress, and leukocyte telomere length (LTL) has been shown to be a surrogate marker of cellular aging. Telomere length gets shorter with cell division and cross-sectional and population-based studies have found that telomere length is progressively shorter with advancing age (1,2). The greatest amount of telomere length attrition happens in the first years of life as growth is accelerated during this time period (1,3,4). Telomeres are also particularly sensitive to reactive oxygen species damage and as such disease conditions associated with inflammation such as chronic stress, metabolic and cardiovascular diseases are associated with shorter telomere length (5,6).

Previous longitudinal studies have found that shorter LTL is predictive of incident diabetes mellitus (7,8) and cardiovascular disease (9). Reactive oxidative species exposure can result in leukocyte telomere damage setting in motion a cascade of events leading up to increased risk for disease states. Shorter telomere length and cellular senescence may result in impaired insulin secretion and insulin resistance as well as the accumulation of senescent cells common in atherosclerosis (7,9).

Leukocyte Telomere Length, Weight and Metabolic Health

Lifestyle factors and genetics both contribute to LTL maintenance suggesting a complex interface between environmental exposures, LTL and disease states. Meta-analyses show
cross-sectional relationships between higher body mass index and certain dietary factors (e.g. sugar-sweetened beverages, processed meats) predicting shorter LTL (10,11). In addition to shorter LTL, the pace of LTL attrition may be correlated with metabolic health, although few studies have examined this over time. Our previous study with obese and overweight Latina women found that rapid LTL shortening was associated with incident hypertension. (12)

Additionally, our clinical trial of weight loss found that individuals who lost at least 10% of their body weight and maintained it for one year had greater LTL lengthening, relative to those who did not maintain weight loss (13). Other longitudinal studies with overweight and obese participants have similarly found that weight loss can result in leukocyte telomere length lengthening (14-16). These studies suggest that changes in nutritional status or adiposity may influence telomere stability.

**Leukocyte Telomere Length, Psychological Health and Behavior Change**

Many studies have shown that longer LTL is associated with better psychological and mental health (17, 18), yet few studies, however, have tested whether LTL impacts behavior or if LTL can be a predictor of behavior change during interventions. Studies suggest that longer LTL is associated with optimism and higher emotional intelligence (19, 20), potentially positive indicators for response to behavior interventions. There is some evidence indicating that longer LTL may predict better responses to weight loss or nutrition-focused interventions (15) and more salutary stress response reactivity during emotional challenges (21). Given the growing accessibility of measures of telomere length in large populations, it is worth further
exploring whether baseline longer TL indeed predicts positive outcomes from behavioral or medical interventions in a way that may be helpful for identifying high resilience vs. high risk groups.

In this exploratory study, we examined LTL in a racially and ethnically diverse, adult cohort of workers at the University of California, San Francisco (UCSF) Medical Center who drank sugared beverages on a daily basis. This group was more likely to be obese and have insulin resistance at baseline (22). We initially tested the impact of exposure to a workplace-based SSB elimination on metabolic health over a 10-month interval. We documented both a decrease in overall workplace SSB consumption, and in a subset demonstrated reduction in waist circumference and improvement in insulin sensitivity (22). We also measured LTL before and after the intervention allowing us to assess any LTL changes during the intervention. Further, we asked whether baseline LTL predicts positive behavioral and metabolic outcomes.

We hypothesized, however, that an individual's reductions in SSB consumption, and improvements in metabolic health would correlate with slower decline in LTL during this period. We also hypothesized, based on prior data demonstrating longer LTL with better mental and immune health (17, 23) that longer LTL would be associated with a better behavioral response to the intervention.
METHODS

Study Design

The study team enrolled 214 employees at UCSF Medical Center into a metabolic sub-study prior to the roll-out of a university-wide SSB ban beginning on November 1, 2015 (22). We over-sampled lower-income service and manual workers for the study as we anticipated that this group would be at higher risk for baseline SSB consumption and could benefit more from the proposed intervention. The inclusion criteria included self-reported daily SSB consumption over the last three months of at minimum 360mL or 12 fl oz (16). Men and women of all body mass index (BMI) groups (underweight, normal weight, overweight and obese) were eligible for participation in the study. Of the 699 potentially eligible participants, 214 were able to participate in the metabolic sub study based on availability and campus location. Half of the participants were then randomized to an additional brief motivational intervention session focused on SSB reduction which included goal setting and health knowledge as part of the study (n=109). The other half of the participants did not receive any additional intervention beyond exposure to the university wide SSB ban (n=105). All participants were exposed to the university wide SSB ban (22). We used the motivational intervention condition as a covariate in this study as described below. The clinical trial was registered using the ClinicalTrials.gov identifier: NCT02585336 (22).

The UCSF Committee on Human Research approved all aspects of the study and participants provided written signed consent prior to participation (22). As per the study protocol,
participants were assured that their response to surveys and all data would not be shared with their supervisors or be associated with any university record. Participants received $125 ($50 for the baseline visit and $75 for follow-up).

Health and SSB Assessments: At baseline, prior to the rollout of the UCSF SSB sales ban, and 10 months after the intervention, participants completed two in-person health visits at UCSF where 30 mL of fasting blood was drawn by trained research staff. The blood sample was then assayed for 13 lipid and metabolic biomarkers including triglycerides, total cholesterol, high density lipoprotein cholesterol concentration (HDL-C), low density lipoprotein cholesterol concentration (LDL-C), apolipoprotein A1 (ApoA1), apolipoprotein B-100 (ApoB), uric acid, gamma-glutamyl transpeptidase (GGT), alanine transaminase (ALT), hemoglobin A1c (HgbA1c), insulin, glucose, and homeostatic model assessment (HOMA). During the same research visit, trained staff measured weight, waist circumference, height for BMI, and drew additional blood for future LTL analysis. After the research visit, samples were immediately processed and aliquoted into serum, plasma, and whole blood, and frozen at –80°C for analysis by the research laboratory of Peter Havel, DVM, University of California, Davis and the Blackburn Lab at University of California, San Francisco. SSB consumption at baseline and at 10-months post-intervention was measured using the modified Beverage Intake Questionnaire-15 (24), which was then used to estimate ounces of SSB intake. We measured SSB consumption both 6 months and 12 months after baseline. Two-hundred and two (94.4%) of participants completed both study visits. There were 182 participants who had LTL and other biological markers measured at baseline and subsequently at follow-up. As previously described (22), reasons for incomplete
follow-up for blood draw were schedule conflicts or lack of interest. There were no statistically significant differences in age, gender, race/ethnicity or BMI at baseline between those who completed both blood draws and those who did not. Further details of methodology used are included in the online supplement of the published trial (22).

**LTL measurement:** LTL was measured from the whole blood collected during the study visit. The UCSF telomere measurement lab uses a quantitative polymerase chain reaction (qPCR) method adapted from Cawthon (2018) (25) to measure LTL (26). The method represents a ratio of two qPCR reactions: telomere over single gene copy (or T/S ratio) and had an interassay coefficient of variation (CV) of 3.4± 3.0%.

**Statistical analysis**

We assessed normality of our outcomes of interest - baseline LTL, changes in LTL and changes in SSB consumption using graphical assessments of normality as well as statistical tests such as Shapiro-Wilk using a cut-point of p<0.05 to reject the null hypothesis that the data are normally distributed. LTL at baseline was normally distributed, but changes in LTL and SSB from baseline to follow-up were not normally distributed. As such, we assessed SSB consumption patterns and metabolic changes in relation to LTL at baseline and changes in LTL and SSB over time using parametric and non-parametric tests to assess associations, including the following parametric tests: student’s t-test for categorical predictors, Pearson’s correlation coefficient (r) for continuous predictors and the respective non-parametric equivalents, Spearman rank-order correlation test, and Mann-Whitney U-test. Specifically, we assessed SSB consumption patterns
and metabolic changes in relation to LTL at baseline and changes in LTL over time and LTL and metabolic changes in relation to SSB consumption. Variables that were significant at $p < 0.10$ and associated with changes in LTL and SSB were included in multivariable linear regression models.

All statistical models were adjusted for participant age, sex, and race/ethnic background, given the associations between these demographic factors and prior studies of LTL (21). Models also adjusted for intervention group in multivariable analyses since those who were randomized to the brief motivational intervention described above report lower SSB intake at baseline.

Multivariable linear regression was used to assess risk factors changes in SSB consumption over the follow-up period and leukocyte telomere attrition rate over 10 months. A sensitivity analysis was conducted by comparing the results with those obtained from robust linear regression to ensure that outliers were not driving the associations.

Multivariable linear regression residuals for LTL change was not normally distributed as per residuals. As such, we used bootstrapping to increase the overall sample size to 1000 to assess normality of the distribution with bootstrapped data, finding that the data was normally distributed and results were unchanged in the larger, bootstrapped sample. We used similar graphical assessments of normality and statistical tests (Shapiro-Wilk) as described above in bivariate analyses. We concluded that the non-normality of the original distribution was related only to our sample size and not to other aspects of the data structure. Therefore, we opted for multivariable linear regression in our analyses.
Change in LTL from baseline to follow-up was adjusted for baseline LTL by assessing percentage change from baseline. We also compared findings with change from baseline to follow-up adjusted for length of follow-up and baseline LTL as not all participants had blood drawn on the exact same day. As there were no significant differences in findings, we present percentage change from baseline as our outcome of interest. HDL-C and ApoA1 were also not included in the same multivariable models due to co-linearity between these variables (R>0.8). Collinearity was assessed using all pairwise correlation coefficients. Data was analyzed using Stata 15.0 and results are presented as means +/- standard deviation (SD).

RESULTS

The current study included participants of a mean age of 41.20 ± 11.04 years. The cohort was 57.94% female, 14.95% non-Hispanic African-American, 21.96% non-Hispanic white, 27.10% non-Hispanic Asian and 19.63% Latino (Table 1). At baseline, mean BMI was 29.39 ± 6.548 kg/m², and 33% were overweight (25 kg/m²<=BMI<30 kg/m²) and another were 39.5% obese (BMI >=30 kg/m²) with the remainder being in the normal weight and underweight category BMI< 25 kg/m². Participants in the current study reported a reduced SSB intake from a mean (SD) of 1052.8 (804.4) mL (35.6 [27.2] fl oz) at baseline to 558.9 (615.1) mL (18.9 [20.8] fl oz) per day 6 months after the sales ban or a decline of 48.6% (16). As reported earlier (16), there was no weight loss or BMI loss (0.03±1.32) on average across the sample: However, there was a significant decrease of 2.19 ± 4.97 cm in mean waist circumference from baseline to follow-up (Table 1).
Telomere Length at Baseline

As expected, longer LTL at baseline was associated with younger age (R=-0.49; p<0.10) and was longer for women (1.07 ± 0.16 versus 1.01 ± 0.17 T/S; p<0.01) (Table 1). Longer LTL at baseline was not associated with SSB intake at baseline (R= 0.06, p=0.41; Table 1). Longer LTL at baseline was associated with lower waist-hip ratio (p<0.001) and trended towards lower waist circumference (p=0.10) and body mass index (BMI) (p=.10) (Table 1) but these associations were no longer significant in multivariable model adjusting for age, race/ethnicity and gender.

BMI, waist circumference and sagittal diameter at baseline were negatively correlated with changes in SSB consumption overall the follow-up period (Beta=-0.16, p=0.04; Beta=-0.14 p=0.06; and Beta=-0.013, p=0.08 respectively; Table 2). Leukocyte telomere length at baseline was negatively correlated with changes in SSB consumption and trended towards statistical significance (Beta=-0.12, p=0.10) (Table 2). In a multivariable model adjusting for variables <=0.10 including race/ethnicity, age, gender, study assignment, Apo B protein at baseline and LTL at baseline, only LTL at baseline was associated with SSB reduction during the follow-up period (Beta=-29.67, 95%CI -57.82-(-)1.51 (Table 3).

Telomere Length Attrition and Changes in SSB and Metabolic Health

Mean LTL at baseline was 1.05 ± 0.17 T/S and at follow-up was 1.04 ± 0.17 T/S, and mean attrition was -0.004 ± 0.07 T/S. Thus, there were no mean changes in LTL over the 10 months, despite the group’s overall improvement in SSB intake and waist due to environmental
intervention. We also categorized by level of change: Forty-four participants (24.2%) reported LTL gain (defined as change >=5%) with a mean increase of 10.8% ± 5.7 %. Eighty-six participants (47.3%) reported LTL maintenance (change >-5% and <5%) with mean maintenance being less than 1% change ((-)0.79 ± 2.7%). Fifty-two (28.6%) reported LTL loss (change <=-5%) with mean loss of -9.2 ± 3.1%.

LTL attrition rate was associated with metabolic changes. In bivariate analysis, decreases in waist circumference were associated with reduced LTL attrition rate (Rho = -0.17; p = 0.03) and decreases in HDL-C and ApoA1 neared statistical significance for association with reduced attrition (Rho = -0.14; p=0.07 and Rho = -0.14; p = 0.05) (Table 4). There was no association between LTL attrition rate and change in BMI over the follow-up period (p=0.37; Table 4).

In a multivariable analysis adjusting for participant’s age, gender and race/ethnicity and group assignment, variables that were independently associated with increases in LTL or slower rates of attrition were decreases in waist circumference (Beta = -0.27, p = 0.03), decreased HDL-C (Beta = -0.20; p = 0.05), and decreased ApoA1 (Beta = -0.09; p = 0.01) (Table 5).

DISCUSSION

This exploratory study examined baseline LTL and 10-month change in LTL in relation to changes in SSB intervention, waist and weight and metabolic change during a healthy beverage initiative intervention. This is the first study that has evaluated LTL changes in the context of an SSB intervention. We evaluated the relationship between LTL and metabolic changes over 10-
months in a group of middle-aged adults, the majority with obesity or overweight. In the context of studies that suggest longer LTL may be a marker of psychological health and optimism (17-20), this is the first study to evaluate the role of LTL to predict behavioral response to an SSB intervention (reduction in SSB consumption).

There was no mean change in LTL and no association between change in SSB intake and change in LTL. Approximately half of participants showed LTL maintenance (within 5% of their baseline; 86/182, 47%) which is similar to other studies that have assessed short term LTL change over a one-year time period (28) and over 2.5 years (29). Our previous studies using 24 and 48 dietary recalls have found cross-sectional associations between higher SSB consumption and shorter LTL (30, 31) and longitudinal associations between reductions in SSB consumption and LTL lengthening (32). It is possible that differences in methods used (dietary recall versus beverage frequency questionnaire) could explain disparate findings. Alternatively, we purposively sampled a population with a high reported consumption of SSB and we may have less variance in overall SSB consumption patterns compared with our previous studies.

However, slower attrition (or lengthening) was associated with decreases in waist circumference (Beta = -0.27, p = 0.03), and decreased ApoA1 (Beta = -0.09; p = 0.01), as well as decreased HDL-C (Beta = -0.20; p = 0.05) (Table 5). A number of cross-sectional studies have found shorter leukocyte telomere length associated with greater abdominal adiposity (33, 34) as did one of our previous longitudinal ones (35). Attenuated LTL loss or slowed aging, is an important, under-recognized benefit of waist circumference loss. Furthermore, waist
circumference loss is correlated with important metabolic changes and benefits, more so than loss of BMI (36). LTL is sensitive to inflammatory processes and ROS damage and as such waist circumference changes may be more reflective of metabolic impact on LTL. The slower attrition patterns associated with decreases in HDL, while seemingly counterintuitive, could be metabolic responses to the SSB intervention, which we speculate on below.

*Leukocyte Telomere Length as a Predictor of Response to SSB Intervention*

Secondly, we asked whether having long telomeres may be a proxy factor for having a greater ability to benefit from an intervention, as suggested by several earlier studies. In terms of health, we found that longer baseline LTL predicted decreases in triglycerides and increases in beneficial lipoproteins including HDL and ApoA1 in the context of a workplace sales ban. Longer LTL was also predictive of lower SSB consumption in our cohort over the follow-up, independent of whether they were assigned to the brief motivational intervention or not. Other intervention studies have found that long LTL is associated with a better intervention/treatment effect, including studies that have focused on weight loss (15), reduction in metabolic markers such as fasting glucose (37), the impact of statins on cardiovascular disease (38), as well as studies that evaluated the role of selective serotonin reuptake inhibitors (SSRIs) and other treatments for depression (39, 40). In other prospective studies, longer LTL has been found to be associated with slower progression of the metabolic syndrome (41) and reduced risk for new onset diabetes mellitus (42). It is possible that any inflammatory or pro-cytokine processes that shorten LTL may have an impact on mood and function, including impetus for behavioral and dietary change. Alternatively, longer baseline
telomere length may be suggestive of a strong immune system and is associated with lower levels of clinical depression and depressive symptoms (17, 23).

A recent experimental study found that longer buccal telomere length was associated with activation in the amygdala and cuneus region of the brain related to an emotional cue, suggesting that telomere length predicts emotional brain activity and connectivity (43). Longer telomere length could suggest that potential of brain cells to engage in action potential, such as that necessary to respond to a cue as part of behavior intervention. Further, additional studies are needed to assess the role that leukocyte and other telomere lengths could play to inform behavioral responses.

Consistency with the Metabolic Attrition Hypothesis

The relation between telomere change and HDL is worth some speculation. Our results may be fit speculations made by Casagrande and Hau (2019) (44) on the role of telomere length attrition processes in the regulation of metabolic signaling and function. They hypothesize that in times of emergency, energy demands such as increased exercise, caloric restriction, or disease states, telomeres are shortened as a way to redirect energy to critical processes. For instance, increased apoA1 and HDL-C in relation to accelerated LTL loss may signal increased energy demands related to the physiological stress of waist circumference loss in the context of SSB reduction. Alternatively, short term intense stress exposure can increase HDL cholesterol in contrast with longer term chronic stress exposures increasing, cortisol, LDL and triglycerides (45, 46). Previous studies have shown that in the context of active weight or adiposity loss,
there is reduced lipoprotein synthesis with impaired very low LDL (VLDL) catabolism resulting in decreased plasma HDL concentrations (47). It is possible that in the context of waist circumference loss due to declines in SSB intake, our participants were in the stage of active adiposity loss. Previous studies have also found reduced HDL levels in the context of SSB or fructose reduction (48). Alternatively, HDL and components such ApoA1, as part of the innate immune system, can also become pro-inflammatory or dysfunctional in the context of increased inflammation (49). Unfortunately, we did not assess changes in inflammatory markers.

Limitations

Future studies evaluating LTL in the context of SSB or other dietary interventions should assess inflammatory changes including C-reactive protein (CRP) and alpha-1-acid glycoprotein (ARP) and provide a more detailed assessment of dietary intake including total energy intake and overall diet quality. While our study also focused on heavy adult SSB consumers, future studies should also assess the impact of SSB interventions in children, adolescents and among adults with varying levels of consumption. Lastly, we conducted a number of statistical tests of association as an exploratory approach to understanding the relationship between an SSB intervention and LTL changes. As such, our findings may be at risk for a Type I error and all interpretation of conclusions should take this into consideration.
CONCLUSIONS

Baseline LTL may be useful in predicting behavioral response for dietary interventions. In our study, longer baseline LTL predicted greater reported reductions in SSB intake.

Abdominal weight loss, a significant finding of our SSB intervention, also paralleled attenuated declines in leukocyte telomere length, emphasizing the important role of adiposity loss in the context of whole-body health.

Future studies with more comprehensive nutritional and inflammatory assessments will be necessary to evaluate the how LTL, stressors, biomarkers, and energy demands and changes in these parameters impact long-term health.

Statement of Authors Contributions to Manuscript:

JW, EE, RL, KS and LS designed the research,
AH, AM conducted research
JL did laboratory analysis
JW and LJ did statistical analysis
All authors approved the final content
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Table 1: Demographic, Metabolic Markers, SSB Consumption and Baseline Leukocyte Telomere Length

| Demographics | Population Mean ±SD at Baseline | Population Change^ Or % | Telomere Mean ±SD (T/S ratio) | P-value Or R (correlation) |
|--------------|---------------------------------|-------------------------|-------------------------------|---------------------------|
| Participant age (years) | 41.20±11.04 | -0.49 | <0.01 |
| Gender | | | | 0.01 |
| Female | 57.94% | 1.07±0.16 | |
| Male | 42.06% | 1.01±0.17 | |
| Race/ethnicity | | | | 0.67 |
| Caucasian | 21.96% | 1.03±0.18 | |
| African-American | 14.95% | 1.02 ±0.16 | |
| Latinx | 19.63% | 1.04 ±0.17 | |
| Asian | 27.10% | 1.07±0.17 | |
| other or unknown | 16.36% | 1.06±0.15 | |
| Adiposity | | | | |
| BMI (kg/m²) | 29.39±6.48 | 0.03±1.32 | -0.05 | 0.51 |
| Waist circumference (cm) | 98.65±16.71 | -2.19±-4.97 | -0.12 | 0.10 |
| Sagittal diameter (cm) | 24.69±5.54 | -0.40±2.23 | -0.12 | 0.10 |
| Waist-Hip ratio | 0.93±0.09 | 0.003±-0.06 | -0.19 | <0.001 |
| Metabolic Control | | | | |
| Uric Acid (mg/dL) | 6.11±1.88 | -0.13±1.08 | -0.04 | 0.53 |
| GGT (U/L) | 37.34±40.61 | 0.67±35.08 | -0.06 | 0.40 |
| ALT (U/L) | 33.60±20.18 | 2.17±27.10 | -0.02 | 0.79 |
| HbA1c (%) | 5.91±0.88 | 0.04±0.42 | -0.06 | 0.39 |
| Insulin (ml U/L) | 19.23±12.97 | 0.30±11.05 | -0.05 | 0.51 |
| Glucose (mg/dL) | 97.11±12.46 | 0.39±8.17 | -0.09 | 0.20 |
| HOMA | 4.74±3.60 | 0.11±3.54 | -0.06 | 0.42 |
| Lipids | | | | |
| Triglycerides (mg/dL) | 110.40±62.28 | -2.11±50.64 | 0.11 | 0.12 |
| Total cholesterol (mg/dL) | 185.4±36.0 | 3.85±23.13 | 0.01 | 0.84 |
| HDL-C (mg/dL) | 45.9±12.3 | 1.53±6.43 | 0.05 | 0.50 |
| LDL-C (mg/dL) | 117.0±29.1 | 3.10±21.18 | -0.03 | 0.68 |
| ApoA1 (mg/dL) | 148.0±30.0 | 3.21±17.60 | 0.03 | 0.01 |
| ApoB (mg/dL) | 71.8±19.3 | 1.32±11.61 | 0.007 | 0.92 |
### SSB Consumption

| SSB Consumption (oz) | 35.6±27.1 | -17.04±28.86 | 0.06 | 0.41 |

### Study Assignment

| Treatment          | Intervention | Control |
|--------------------|--------------|---------|
| Mean               | 1.08±0.18    | 1.02±0.16 |
| Change             | <0.01        |         |

^ Change is defined as follow-up value-baseline value

ALT, Alanine Aminotransferase; ApoA1, Apolipoprotein A1; ApoB, Apolipoprotein B; BMI, body mass index; GGT, Gamma-glutamyl transferase; HbA1c, hemoglobin A1c; HDL-C, high-density lipoprotein cholesterol; HOMA-IR, homeostatic model assessment insulin resistance; LD-CL, low density lipoprotein cholesterol; SSB, sugar sweetened beverage
### Table 2: Metabolic Markers, Leukocyte Telomere Length and Changes in SSB Consumption Over 6 Months

|                      | SSB Mean ±SD   | P-value       |
|----------------------|----------------|---------------|
|                      | Or Rho (spearman’s correlation) |               |

#### Demographics

|                              |                |               |
|------------------------------|----------------|---------------|
| Participant age (years)      | -0.07          | 0.31          |
| Gender                       | 0.55           |               |
| Female                       | -14.47±27.14   |               |
| Male                         | -20.88±31.03   |               |
| Race/ethnicity               |                |               |
| Caucasian                    | -13.99±19.28   | 0.47          |
| African-American             | -16.88±29.81   |               |
| Latinx/Hispanic              | -25.78±31.22   |               |
| Asian                        | -14.38±34.25   |               |
| other or unknown             | -15.88±28.80   |               |

#### Adiposity

|                               |                |               |
|-------------------------------|----------------|---------------|
| BMI (kg/m²)                   | -0.16          | 0.04          |
| Waist circumference (cm)      | -0.14          | 0.06          |
| Sagittal diameter (cm)        | -0.13          | 0.08          |
| Waist-Hip ratio               | -0.08          | 0.26          |

#### Metabolic Control

|                                 |                |               |
|---------------------------------|----------------|---------------|
| Uric Acid (mg/dL)               | -0.01          | 0.89          |
| GGT (U/L)                       | -0.10          | 0.15          |
| ALT (U/L)                       | -0.01          | 0.86          |
| HbA1c (%)                       | -0.09          | 0.22          |
| Insulin (ml U/L)                | 0.02           | 0.73          |
| Glucose (mg/dL)                 | -0.09          | 0.23          |
| HOMA-IR                         | -0.04          | 0.60          |

#### Lipids

|                                |                |               |
|--------------------------------|----------------|---------------|
| Triglycerides (mg/dL)          | -0.09          | 0.24          |
| Total cholesterol (mg/dL)      | 0.11           | 0.14          |
| HDL -C (mg/dL)                 | 0.04           | 0.60          |
| LDL-C (mg/dL)                  | -0.08          | 0.24          |
| ApoA1 (mg/dL)                  | 0.05           | 0.51          |
| ApoB (mg/dL)                   | **-0.12**      | **0.10**      |

#### Telomere Length

Downloaded from https://academic.oup.com/cdn/advance-article/doi/10.1093/cdn/nzab084/6284782 by guest on 29 May 2021
Leukocyte Telomere Length
(baseline) (T/S ratio) -0.12 0.10

Acronyms: ALT, Alanine Aminotransferase; ApoA1, Apolipoprotein A1; ApoB, Apolipoprotein B; BMI, body mass index; GGT, Gamma-glutamyl transferase; HbA1c, hemoglobin A1c; HDL-C, high-density lipoprotein cholesterol; HOMA-IR, homeostatic model assessment-insulin resistance; LDL, low density lipoprotein cholesterol; SSB, sugar-sweetened beverage.
| Demographics                      | Unstandardized | P-value  | 95% CI       |
|----------------------------------|----------------|----------|--------------|
| **Participant age**              | -0.27          | 0.25     | -0.72, -0.19 |
| Female                           | -7.82          | 0.59     | -16.35, 0.72 |
| **Study assignment**             | -13.98         | <0.01    | -22.37, -5.58|
| **Race/ethnicity**               |                |          |              |
| Caucasian                        | 1.0            |          |              |
| African-American                 | -1.49          | 0.83     | -15.52, 12.53|
| Latinx/Hispanic                  | -3.06          | 0.65     | -16.16, 10.04|
| Asian                            | -1.08          | 0.85     | -12.30, 10.14|
| Other/unknown                    | -1.21          | 0.86     | -14.68, 12.27|
| **Adiposity**                    |                |          |              |
| BMI (kg/m2)                      | -0.40          | 0.12     | -1.08, (-)0.27|
| **Lipids**                       |                |          |              |
| ApoB (mg/dL)                     | -0.06          | 0.62     | -0.29, 0.17  |
| **Telomere Length**              |                |          |              |
| Baseline Leukocyte Telomere Length (T/S) | -29.67        | 0.04     | -57.82, -1.51|

*All variables in the table are included in the multivariable regression model
ApoB, apolipoprotein B; BMI, body mass index; SSB, sugar sweetened beverage
Table 4: Change in in Metabolic Markers* and SSB Consumption in Relation to Leukocyte Telomere Length Percentage Attrition ^

| Demographics | Mean +/-SD | P-value |
|--------------|------------|---------|
| Participant age (years) | -0.08 | 0.26 |
| Gender | | |
| Female | -1.17±8.07 | |
| Male | 0.71±-8.22 |
| Race/ethnicity | | |
| Caucasian | -0.43±7.46 | 0.69 |
| African-American | 0.25±-9.87 | |
| Latinx/Hispanic | 0.80±8.27 | |
| Asian | -0.56±-6.95 | |
| other or unknown | -1.88±-9.18 | |
| Adiposity | | |
| BMI (kg/m2) | -0.07 | 0.37 |
| Waist circumference (cm) | -0.17 | 0.03 |
| Sagittal diameter (cm) | -0.12 | 0.13 |
| Waist-Hip ratio | -0.08 | 0.29 |
| Metabolic Control | | |
| Uric Acid (mg/dL) | -0.12 | 0.12 |
| GGT (U/L) | 0.03 | 0.73 |
| ALT (U/L) | 0.02 | 0.77 |
| HbA1c (%) | 0.04 | 0.62 |
| Insulin (ml U/L) | -0.001 | 0.98 |
| Glucose (mg/dL) | -0.04 | 0.57 |
| HOMA | -0.02 | 0.83 |
| Lipids | | |
| Triglycerides (mg/dL) | 0.08 | 0.27 |
| Total cholesterol (mg/dL) | -0.07 | 0.32 |
| HDL -C (mg/dL) | -0.14 | 0.07 |
| LDL-C (mg/dL) | -0.11 | 0.13 |
| Apo A protein (mg/dL) | -0.14 | 0.05 |
| Apo B protein (mg/dL) | -0.07 | 0.37 |
| Change in SSB | | |
| SSB Consumption (ounces) | 0.10 | 0.22 |
^ Percentage attrition is (LTL Follow-Up-TL Baseline)/TL Baseline *100
Abbreviations: ALT, Alanine Aminotransferase; ApoA1, Apolipoprotein A1; ApoB, Apolipoprotein B; BMI, body mass index; GGT, Gamma-glutamyl transferase; HbA1c, hemoglobin A1c; HDL-C, high-density lipoprotein cholesterol; HOMA-IR, homeostatic model assessment insulin resistance; LDL-C, low density lipoprotein cholesterol; LTL, leukocyte telomere length; SSB, sugar sweetened beverage.
Table 5: Change in Metabolic Markers* and Leukocyte Telomere Length Percentage Attrition^:
Multivariable Linear Regression Model

| Demographics                  | Beta   | P-value | 95% CI  |
|-------------------------------|--------|---------|---------|
| Participant age (years)       | -0.10  | 0.10    | -0.22, 0.02 |
| Female                        | -1.86  | 0.15    | -4.43, 0.71 |
| Participant race/ethnicity    |        |         |         |
| Caucasian                     | 1.00   |         |         |
| African-American              | 0.66   | 0.31    | -3.55, 4.87 |
| Latinx/Hispanic               | 1.08   | 0.53    | -2.95, 5.10 |
| Asian                         | -0.04  | 0.98    | -3.76, 3.29 |
| Other                         | -1.55  | 0.46    | -5.16, 2.98 |
| Group assignment              | -2.48  | 0.06    | -5.02, 0.06 |

| Adiposity                     |        |         |         |
| Waist circumference (cm)      | -0.27  | 0.03    | -0.52, -0.02 |
| Lipids                        |        |         |         |
| HDL-C (mg/dL)                 | -0.20  | 0.05    | -0.39, 0.002 |
| ApoA1 (mg/dL)                 | -0.09  | 0.01    | -0.16, -0.02 |

*All variables in the table are included in the multivariable model with the exception of HDL and Apo A protein which were included in separate models due to collinearity
^Percentage attrition is (TL Follow-Up-TL Baseline)/TL Baseline *100
Abbreviations: ApoA1, Apolipoprotein A1; HDL-C, high density lipoprotein cholesterol