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Association of an Evolutionary-Concordance Score with Weight Change in the REGARDS Cohort

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B.S.
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Atlanta, GA
2016

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An abstract of
A thesis submitted to the Faculty of the
Rollins School of Public Health of Emory University
in partial fulfillment of the requirements for the degree of
Master of Public Health
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Abstract

Association of an Evolutionary-Concordance Score with Weight Change in the REGARDS Cohort

By Thomas Waltz

Background: The prevalence of obesity has increased substantially worldwide over the past 20 years. Evolutionary-concordance (EC) scores have been used to investigate associations of lifestyle and dietary patterns with health outcomes. However, there are no reported studies of associations of evolutionary-concordance dietary and lifestyle scores with weight change.

Methods: We analyzed data from 9,472 Black and White men and women in the prospective REGARDS cohort with baseline (2003–2007) and 10-year follow-up anthropometrics. Baseline information also included sociodemographic, medical, lifestyle, dietary (via a Block98 food frequency questionnaire), and psychosocial characteristics. We calculated a four-component (alcohol intake, physical activity, sedentary behavior, and social network size) EC lifestyle score, a 13-component EC diet score, and a five-component total EC score (the four lifestyle components plus the EC diet score as the fifth component), such that higher scores indicated higher evolutionary concordance. We used multivariable general linear models to calculate adjusted mean absolute and proportional 10-year weight changes according to baseline EC score quintiles.

Results: Crude and adjusted mean and proportional weight and BMI changes in all score quintiles were small (mean changes: $\leq$ 0.85 kg; proportional changes: < 1%). There were no substantial or clear patterns of differences across the score quintiles. These findings were similar regardless of sex, race, or baseline age or smoking or comorbidity status.

Conclusion: Our findings suggest that evolutionary-concordance scores were not associated with weight change over 10 years in the REGARDS cohort, regardless of race, sex and replacement hormone therapy use, age, and baseline smoking or comorbidity status. Further studies of associations of evolutionary-concordance dietary and lifestyle pattern scores with weight change in populations with more substantial long-term weight change are needed.

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Introduction

Obesity is a complex, multifactorial disease which, while largely preventable, has substantially increased in prevalence within the United States (US) over the past 20 years[1]. More than two-thirds of US adults are currently overweight or obese[1], while globally, the estimated prevalence of obesity or overweight is over one-third of the population[2]. If modern trends continue, it is estimated that 38% of the world's population will be overweight and 20% will be obese by 2030[3]. With obesity being a well-known risk factor for multiple diseases and disorders, including Type 2 diabetes mellitus, cardiovascular disease, and certain types of cancer, concerns are rising regarding the future humanitarian toll obesity-related chronic diseases could have[1,4].

Economic impacts are also of concern. Medical costs associated with obesity range as high as $209.7 billion in the United States, with much of the cost attributable to treating obesity-related comorbidities such as cardiovascular (CVD) disease ($193–$315 billion) and Type 2 diabetes mellitus ($105–$245 billion)[5]. Obesity was estimated to cost between an average of 0.8% and 2.42% of gross domestic product across eight countries in 2019, and if the status quo is not changed by 2060, the economic impact of obesity is projected to grow to 3.6% of GDP[6].

Previous epidemiological studies have attributed the rise in obesity in the United States to modifiable behaviors, including poor diet, lack of physical activity, and sedentary behavior[7,8]. For instance, one 2017 meta-analysis of 35 human studies that reported on an association of diet with overweight/obesity risk found that individuals in the highest (most adherent) relative to the lowest category of a "prudent/healthy diet" score had 36% lower risk of overweight/obesity (OR = 0.64; 95% CI 0.52-0.78)[9]. In the same meta-analysis, individuals in the highest (most unhealthy) relative to the lowest category of an "unhealthy/Western diet" score had 65% higher risk of obesity/overweight (OR = 1.65; 95% CI 1.45 – 1.87); $P < 0.0001$)[9]. Individual studies have also found that unhealthier or lower quality diets, measured through both dietary scores and individual foods, are associated with overweight/obesity and weight gain[10-12]. Specifically, potato chips, unprocessed red meat, sugar-sweetened beverages, and fast food have been implicated in weight gain and the development of obesity[12,13]. However, results, especially regarding sugar-sweetened beverages, have been inconsistent[14], indicating the need for clarifying studies.

The association of diet with obesity makes sense from a biological perspective. For instance, Ochner et al. describe that excess energy intake may lead to more and larger fat cells, and this increase in fat cell number may occur in overweight individuals[15,16]. Hargrave et al. state that prolonged consumption of western diets (high in saturated fats and sugar) damage the hippocampus, which may inhibit individuals' ability to resist environmental-food related stimuli eliciting appetitive behaviors, resulting in positive energy balance and weight gain[17]. Neuronal reward-related signaling pathways can also override homeostatic and inhibitory pathways, driving higher versus lower calorie food intake[18,19], potentially driving a cycle in which neuronal pathways become dysregulated. Endocrinologically, diets high in fat trigger central and peripheral leptin resistance, which has been implicated in the development of diet-induced obesity through down-regulation of cell leptin receptors[20]. It has also been posited that leptin resistance is dependent on type and duration of diet[21-23], although results regarding which nutrients affect leptin resistance remain inconsistent and require further investigation.

Lack of physical activity has been implicated as a major risk factor for developing obesity, and physical inactivity in adolescence has been associated with adulthood obesity, even when controlling for body mass index (BMI)[24,25]. Obese children and adolescents are also five times as likely to be obese in adulthood compared to those who were normal weight in childhood and adolescence[26]. The synergy between energy intake and physical activity in the regulation of body weight potentially plays an important role[27], highlighting the importance of studying interactions among weight gain risk factors and the development of obesity. From a biological perspective, lack of physical activity can lead to a positive energy imbalance, leading to weight gain over time[28]. Work-related physical activity has declined in the past 50 years, leading to 100 kilocalories (kcal) less energy expenditure per day in men and women, and an association with an increase in mean body weight during this time[29]. Physiologically, low intensity physical activity such as non-exercise ambulatory movements and walking activates lipoprotein lipase (LPL), of which low levels have been associated with lipid partitioning to tissues and obesity in mice models[30]. Specifically, LPL has been shown to decrease 10-fold in oxidative muscles when remaining sedentary for hours[31], implicating modern lifestyles in the development of obesity.

Results from multiple studies indicate that watching television is directly associated with obesity[32-34], although hours of computer-use and reading are not[33]. This could be due to reduced energy consumption and increased snacking while watching TV, leading to a positive energy balance overall[35]. One cross-sectional study of 5,338 adults in Europe, the United Kingdom, and the US found that participants in the highest sitting time quartile (≥ 8 hours of sitting /day) had a 62% higher odds of obesity than participants in the lowest sitting quartile (< 4 hours/day)[36]. Furthermore, due to the increased time spent sitting while awake, humans do not perform thousands of muscle contractions that could contribute to cumulative energy expenditure, which may increase the propensity to become overweight[37].

There are no reported studies that investigated an association of social network size with obesity, although associations of other network characteristics with obesity have been reported. Multiple studies found associations of other characteristics of the networks that people immerse themselves in with their weight and weight influencing behaviors[38–40]. One cross-sectional study that investigated social network characteristics with weight change among 245 African-American and Hispanic adults found that greater weight loss was associated with network members' help in reaching eating and physical activity goals, while weight gain was associated with obese network members living in the home[38]. This study is also the only study we found that addressed social network size, finding that each additional network member was statistically significantly associated with a 0.40 lb. (95% CI 0.16 – 0.64) increase in weight gain after adjustment for age, race/ethnicity, gender, education, study site, and randomization group, although further studies are needed to clarify this association[38]. In a 32-year prospective cohort study of 12,067 participants from the Framingham Heart Study that examined whether weight gain in one individual was associated with weight gain in his or her social network, individuals who had a friend become obese had a 57% higher risk of becoming obese. Individuals with a sibling who became obese had a 40% increase in risk of becoming obese, and individuals with a spouse who became obese had a 37% chance increase in risk of becoming obese[40].

Evolutionary concordance lifestyle scores (ECLS) are used to assess within-study population relative closeness of individuals' diet and lifestyle patterns to more evolutionary concordant patterns, and in turn associations of the scores with various health outcomes[41,42]. More evolutionary concordant behaviors include higher physical activity, less sedentary behavior, limited alcohol consumption, balanced energy intake, not smoking cigarettes, and maintaining a strong social network. Evolutionary-concordant diet patterns are characterized by higher intakes of fruits, vegetables, lean meats, and nuts with less intake of grains, dairy products, fats, sugars, and salt. Previously, Troeschel and colleagues reported that a higher (more evolutionary concordant) relative to a lower ECL score (containing both lifestyle and diet scores), was statistically significantly inversely associated with all-cause, all-cancer, and all-cardiovascular disease risk in the REGARDS cohort[41]. Furthermore, in the Iowa Women's Health Study (n = 35,221 women), the evolutionary-concordance diet score alone was not associated with incident colorectal cancer, but a more evolutionary-concordant lifestyle composed of not smoking, high levels of physical activity, and low body mass index was inversely associated with it[42]. Given its comprehensive inclusion of risk factors relevant to obesity and its associations with other health outcomes, the EC score could address gaps in knowledge regarding the association of lifestyle behaviors and diet with obesity.

Addressing gaps in knowledge regarding associations of lifestyle scores with weight gain is needed. In the three studies we found that investigated an association of a lifestyle score with weight gain, all focused on majority White populations[43-45]. Historically, obesity has been more prevalent in non-White populations[46,47], although these populations are underrepresented in the literature. Furthermore, two of the studies focused on either children and adolescents or on specific university populations and one did not provide details on statistical analyses[43,44]. Only one focused on an association of lifestyle (including diet) with weight gain in adults[45]. All of these studies were cross-sectional, and to our knowledge, no published longitudinal studies investigated an association of evolutionary concordance diet and lifestyle scores, separately or combined, with weight or weight change. Accordingly, for my thesis, I will address these gaps in knowledge by investigating an association of previously-described evolutionary concordance diet and lifestyle scores, separately and combined, with weight or weight change over 10 years of follow-up in the prospective REasons for Geographic and Racial Differences in Stroke (REGARDS) cohort, which comprises 30,239 Black (42%) and White (58%) men and women aged 45 and older from the 48 contiguous states and Washington DC. I will also explore potential differences in the associations among different population subgroups (e.g., sex, race, age) and investigate the relative importance of each EC score component to the estimated associations.

Methods

Study Population

REGARDS (Reasons for Geographic and Racial Differences in Stroke) is a prospective cohort study of 30,239 African-American and White adults aged 45 years or older focused on geographical and racial factors in stroke[48]. Participants were recruited from the United States' 48 contiguous states and Washington DC January 2003 through October 2007 by mail, followed by computer assisted phone interviews (CATI) to determine eligibility and collect information on stroke risk factors, sociodemographics, diet, lifestyle, psychosocial characteristics, and anthropometrics[49,50]. African-American participants and residents of the stroke belt in the Southeastern United States were oversampled by study design[51]. Physical measurements, including height, weight, and abdominal circumferences were performed by trained study staff during an in-home visit, approximately 3–4 weeks after the CATIs. At this visit, participants were also given a previously validated 110-item Block 98 Food Frequency Questionnaire (FFQ) to be self-completed and returned by mail[50]. Total energy and nutrient intakes were estimated by NutritionQuest and calculated by summing food and supplemental sources for each study participant. Several lifestyle exposures were collected during the CATI, including alcohol use, physical activity, smoking history, social network size, and sedentary behavior. Alcohol use was self-reported by answering open-ended questions addressing current alcohol use, measured in drinks per day, week, month, or year[41]. Self-reported physical activity was collected via an open-ended question regarding a participant's frequency of exercise vigorous enough to work up a sweat. Self-reported social network size was calculated as the sum of the number of family and friends the participant felt close to. Sedentary behavior was assessed via self-reported hours of watching TV or video, with response options as none, 1-6 hours/week, 1 hour/day, 2 hours/day, 3 hours/day, or 4+ hours/day.

For the present analyses, we excluded participants with data anomalies (*n* = 56), missing or implausible dietary data (*n* = 8,547) or lifestyle EC components (*n* = 1,835), a body mass index (BMI) <18.5 kg/m^2 (*n* = 207), lost to follow-up (*n* = 168); cancer (other than non-melanoma skin cancer), or end stage renal disease at baseline (*n* = 1963); missing follow-up weight or BMI data (7,924) ; and proportional weight changes over the 10 years of follow-up of > 4.0 standard deviations of the mean in the study population (n = 67); leaving 9,472 participants for analysis **(Fig. 1**). The Institutional Review Boards of all participating institutions approved the original study, and all participants gave verbal and written consent at enrollment.

Calculation of the Evolutionary-Concordance Diet Score

Our primary exposure was a total EC score comprising a 13-component EC diet score as a single component plus four major non-dietary lifestyle components. This score, which in previous reports had additional smoking and adiposity components, was inversely associated with all-cause, all-cancer, and all-cardiovascular disease mortality in REGARDS[41]. For the EC diet score, we categorized dietary elements from the baseline FFQ into 11 groups reflecting gram intakes of different food groups (vegetables, fruits, lean meats, fish, nuts, red and processed meat, dairy, grains and starches, baked goods, sugar-sweetened beverages, and fruit/vegetable diversity) and two groups reflecting milligrams of two micronutrients (sodium, calcium). Vegetable diversity was defined as the sum of the total number of different types of fruits and vegetables that the participant reported eating more than 1–3 times a month. Calcium independent of dairy food intakes was estimated by computing the residuals from a regression model with dairy as the independent variable and calcium intake as the dependent variable. The residuals were then added to the mean calcium intake (mg) for the study population. We categorized intakes of these 11 dietary groupings into sex-specific quintiles based on their distributions in the analytic cohort at baseline. Next, we assigned the quintiles of the exposures for which greater intake was considered more evolutionary-concordant (vegetables fruits, lean meats, fish, nuts, diversity of fruits and vegetables, and calcium) values on an increasing scale of 1 to 5, with 5 reflecting higher evolutionary-concordance. We assigned the quintiles of the exposures for which less intake was considered more evolutionary concordant (red and processed meat, dairy products, grains, baked goods, sugar-sweetened beverages, and sodium) decreasing values from 5 to 1, reflecting decreasing evolutionary concordance. Then, we summed the values for the 11 dietary score components to yield the evolutionary concordance diet score such that a higher score indicated greater evolutionary concordance.

Calculation of the Lifestyle and Total Evolutionary-Concordance Scores

We calculated a 4-component (alcohol intake, physical activity, sedentary behavior, and social network size) EC lifestyle (ECL) score, as described below. Unlike for our previously reported ECL score, we did not include smoking or adiposity components. We excluded smoking because previous literature suggested that smoking status may substantially modify associations of multiple risk factors with weight gain/adiposity[52–54]. We excluded an adiposity measure since this was an outcome, rather than an exposure, for the present study. We categorized the remaining five lifestyle components as follows. We categorized self-reported alcohol intake into five sex-specific categories of 0, > 0 – < 1.0, 1.0 – 3.75, 4.0 – 7.0, and >7.0 drinks per week for men, and 0, > 0.0 – < 0.5, 0.5 – 1.75, 2.0 – 5.0, and >5 drinks per week for women. We assigned the alcohol categories values of 5 – 1, from low to high. We categorized baseline smoking as non-smokers and quartiles of current packs of cigarettes smoked per week among the smokers. This variable was excluded as an ECL score component, but added as a covariate to control for smoking. We categorized social network into quintiles of 0–5, 6–8, 9–11, 12–17, and ≥18 friends and family members participants felt close to, and then assigned each category a value from 1–5, from low to high. We categorized physical activity and sedentary behavior according to their distributions into categories of 0, 1–2, 3–4, 5–6, and ≥7 times exercised per week for physical activity, and <1, 1, 2, 3, or ≥4 hours per day of screen time for sedentary behavior, and then assigned each category a value from 1–5, from low to high. Finally, we summed the values of all four components to constitute the ECL score, with possible values of 4–20, with higher values indicating higher evolutionary concordance.

To calculate a 5-component total EC score, we first categorized the diet score into quintiles with values ranging from 1–5, from low to high. Then, we added these values to those of the EC lifestyle score to constitute the total EC score, with possible values of 5–25, with higher values indicating greater evolutionary concordance.

Outcome Assessment

Limited follow-up data, including measured anthropometrics, were collected at a second in-home visit 10 years after baseline. From the baseline and 10-year follow-up anthropometrics, we calculated absolute and proportional (follow-up - baseline measurement / baseline measurement x 100%) changes in weight and body mass index as our primary outcomes.

Statistical Analyses

We summarized the baseline characteristics of the participants' characteristics overall and across quintiles of the total EC score using descriptive statistics, and compared them using ANOVA for continuous variables and chi-square tests for categorical variables. We also compared the characteristics of cohort participants included in the present study with those who were excluded in a similar manner. To investigate whether more evolutionary-concordant diets and lifestyles, separately and combined, were associated with weight change over 10 years, we used multivariable general linear models to calculate mean absolute and proportional weight changes according to the three EC scores at baseline as continuous variables and categorized according to quintiles. We selected covariates for all models based on biological plausibility and previous literature. All final models were adjusted for age (years), race (Black or White), annual household income (<$20 k, 20 k – $30 k, 35–74 k, ≥ 75 k, missing), education level (less than high school, high school graduate, some college, college graduate and above), marital status (married, single, other), smoking (packs/week), health insurance (yes, no), sex/current hormone replacement therapy use (male, female – hormone therapy, female – no hormone therapy), region of residence (stroke belt, non-stroke belt), total energy intake (kcal/day), and comorbidities at baseline (yes/no). Approximately 10% of participants in our analytic cohort did not report their income, so we used a missing indicator variable for income for these participants in our analysis. All other covariates had < 1% of data missing, so we did not use missing indicator variables for these covariates.

As a secondary analysis, to assess whether the associations of the EC scores with weight change differed according to key participant characteristics, we stratified the above analyses according to categories of age (45–60 years, 60–70 years, and >70 years), smoking status (former, never, or current), sex (male/female), race (Black/White), and presence of a co-morbidity at baseline (yes/no). To test for multiplicative interaction, we first created interaction terms by multiplying continuous variable values for age and smoking, and categorical variable values for race, sex and HRT status, and comorbidity, separately, by total EC score values for each participant to create interaction terms. Then, we included these interaction terms in the multivariable linear regression models.

As sensitivity analyses, to assess 1) whether any individual component of the total EC score primarily drove the association of the score with weight change, and 2) the relative contributions of the scores' components to the estimated associations, we removed and replaced each component one at a time from the total EC score and assessed the associations of each reduced total EC score and its respective removed individual component, adjusted for one another, with weight change. We then calculated proportional differences in the average absolute and proportional BMI change of the highest relative to the lowest quintile of each reduced ECL score to that of the full ECL score through the following equation: $\frac{\beta - \beta\prime}{\beta} * 100$, where β' represents the average absolute or proportional weight change between the highest and lowest quintiles of reduced EC score and β represents the average absolute or proportional weight change between the highest and lowest quintiles of the full EC score.

We conducted all statistical analyses using SAS version 9.4 (SAS Institute) statistical software. We considered two-side P-values ≤0.05 and 95% confidence intervals (CI) that excluded 1.0 statistically significant.

Results

Over a mean follow-up time of 9.3 years, 2,780 (29.4%) participants gained weight, defined as gaining more than 3% of body weight over follow-up, 4,023 (42.5%) participants lost weight, defined as losing more than 3% of body weight over follow-up, and 2,669 (28.2%) participants maintained weight, defined as gaining or losing less than 3% of body weight over follow-up. Selected characteristics of the participants at baseline according to total EC score quintiles are summarized in **Table 1**. Participants in higher relative to the lower quintiles of the full EC score were more likely to be older, White, married, have health insurance, higher income, lower BMI, lower waist circumference, higher EC diet score, a larger social network, take HRT (among women), not smoke, consume less alcohol, exercise more frequently, and watch less TV at baseline. There were no differences in region of residence or baseline comorbidity status among individuals in higher relative to lower EC score quintiles. As shown in **Supplemental Table 1**, participants who attended the second in-home visit and had follow-up data on weight were more likely to be younger, White, married, female, have health insurance, higher income, lower total energy intake, consume more alcohol, exercise more frequently, and watch less TV at baseline than individuals who attended only the first in-home visit (all $P < 0.01$). Individuals who returned for the second in-home visit were also less likely to have comorbidities than those who did not ($P < 0.01$). Also, there was no difference in mean social network size at baseline among individuals who attended the second in home visit and those who did not.

Mean absolute and proportional weight and BMI changes over 10 years across total evolutionary-concordance score quintiles are shown in **Table 2**. All crude and adjusted mean changes in all score quintiles were small (e.g., all mean absolute weight changes were ≤0.85 kg (1.9 pounds), and all proportional weight and BMI changes were <1%), and despite the statistically significant P_{trends} in some adjusted values, there were no substantial or clear patterns of differences across the score quintiles. The results from the analyses using the total EC score as a continuous variable mirrored those from the quintile analyses. These findings were similar regardless of smoking status, race, age, sex, and comorbidity status at baseline (**Supplemental Tables 3 – 7**). The findings for the EC lifestyle score and EC diet score were similar to those for the total EC score (**Tables 2 – 4).**

Supplemental Analyses

Multivariable-adjusted mean absolute and proportional weight and BMI changes over 10 years among those in the highest relative to the lowest quintiles of the total evolutionary-concordance score, overall and after removing and replacing each of its five components one at a time are shown in **Supplemental Table 8**. All estimates from the five reduced scores were small and did not differ substantially from those for the original 5-component total EC score.

Discussion

Contrary to our hypothesis, our findings suggested that more evolutionary concordant lifestyles and diets, separately and combined, were not associated with weight change over 10 years in the REGARDS cohort, regardless of race, smoking status, sex, age, or comorbidities. Importantly, the overall mean weight change (gain) in this cohort was very small and did not substantially differ across evolutionary-concordance score quintiles. Such overall minimal weight change in the cohort may have prohibited us from identifying factors that could substantially affect long-term weight change. To our knowledge, this is the first large prospective study of associations of evolutionary-concordance diet and lifestyle scores with long-term weight change in a diverse population.

Results regarding the biological plausibility of the association between EC score components and weight loss are mixed, and further research is required to corroborate findings regarding most components. In one systematic review of 14 prospective cohort studies that investigated associations of vegetable intakes with weight outcomes, higher vegetable intakes were associated with either weight loss or lower risk of weight gain and obesity in 10 of the 14 studies[55]. Four of these studies found statistically significant trends for lower risk for obesity and weight gain with higher vegetable intakes. While grain intakes are considered not to be evolutionarily-concordant in the EC diet score, higher whole grain intakes have induced weight loss in one study. One randomized cross-over study of 60 obese Danish adults at risk for developing metabolic syndrome that tested the effect of whole grain diets on weight loss over eight weeks found that a whole grain diet induced weight loss over an eight-week period (weight change: -0.2 kg; $P<0.0001$)[56]. Wu et al. postulated this was through an abundance of dietary fiber contents in whole grain diets, which increase satiety and energy expenditure while simultaneously decreasing energy absorption and fat storage[57]. A meta-analysis of 18 prospective cohort studies (n=113,477) found that the highest relative to the lowest quantile of red and processed meat intakes were statistically significantly associated with risk for obesity (OR =

1.37; 95% CI 1.14 – 1.64) and waist circumferences (OR = 2.75; 95% CI 2.15 – 3.35), but not BMIs (OR = 1.35; 95% CI 0.98 – 1.71)[58]. Reported associations of alcohol intakes with weight gain have been mixed. Alcohol can suppress lipid oxidation such that fat oxidation does not occur when an increase in fat intake occurs. This non-oxidized fat is then preferentially deposited in the abdominal area[59]. However, a systematic review of 31 cross-sectional and cohort studies found that the results regarding the association of alcohol intake with weight gain were mixed, although studies that focused on higher levels of drinking found a positive association with weight gain[60]. These somewhat inconsistent results could potentially be attributed to the different types of alcoholic beverages examined in the studies, as it found spirits (e.g., vodka, whiskey, tequila, rum, gin) were associated with greater detrimental weight outcomes (increases in BMI and waist circumference) than was wine. Associations of beer with weight change were mixed[60]. Physical activity can play a role in weight change, although weight loss on an individual level is highly heterogeneous[61]. In mice and rat studies, exercise may have influenced appetite through leptin sensitivity or alterations in concentrations of gut-released satiety signals[62,63]. However, the biological mechanisms for physical activity's influence on weight loss remain unclear[64], especially given the mixed results in studies that investigated the association of physical activity with weight loss in humans[65,66]. Although less studied, sedentary behavior has not been statistically significantly associated with weight or BMI change in current literature, and only slight differences have been found in amount of sedentary time between obese and normal weight men and women[67,68]. One meta-analysis of 23 prospective cohort studies found no association of sedentary behavior among adults with any measure of body weight, except waist circumference, although absolute change in waist over five years was small (Change in waist circumference = 0.02 cm; 95% CI 0.01 – 0.04; P=0.001)[69]. Social networks may can have important implications into risks of developing overweight and obesity[37-40], although more studies are needed to corroborate these findings.

More studies are needed examining the association of evolutionary-concordant lifestyle scores with weight gain, and diet scores have been associated with less weight gain in multiple studies. Only one study has investigated associations of lifestyle scores with weight gain in young adults. A 2016 pilot cross-sectional study (*n* = 269 students from Utah Valley University) found that scores from the Lifestyle Questionnaire – Weight Management (LQ-WM) instrument (includes healthy and unhealthy weight management practices, dietary habits, difficult or negative emotions while eating, difficult emotional days, self-reported motivation level, and body image concerns) statistically significantly differed among those who lost, maintained, or gained weight during the previous year[43]. Two prospective cohort studies that investigated associations of various diet scores (e.g. Alternate Health Eating Index – 2010, Alternate Mediterranean Diet, Dietary Approaches to Stop Hypertension) with weight and weight change found that adherence to a 'healthier' diet was associated with less weight gain[70,71] Specifically, one prospective study that followed 50,603 women in the Nurses' Health Study and 22,973 men in the Health Professionals Follow-Up Study for 20 years, and 72,495 in the Nurses' Health Study II for 18 years found that a one standard deviation increase in the Alternate Health Eating Index-2010 (comprising vegetable, fruit, whole grain, nut, legume, long chain n-3 fatty acid, n-6 polyunsaturated fat, sugar-sweetened beverage, alcohol, red and processed meat, and sodium intakes) was associated with a 0.47 kg less weight gain among participants over 4-year periods (95% CI -0.66 – -0.28). Associations of the Alternate Mediterranean Diet (aMed) score and the Dietary Approaches to Stop Hypertension (DASH) score with less weight gain over 4-year periods were similar (Difference in weight gain for aMed: -0.23 kg; 95% CI -0.30 – -0.16; Difference in weight gain from DASH: -0.42; 95% CI -0.54 – -0.29)[70]. Another study that investigated associations of six dietary scores (French Programme National Nutrition Santé-Guideline Score [PNNS-GS], Dietary Guidelines for Americans Index [DGAI], Diet Quality Index-International [DQI-I], Mediterranean Diet Scale [MDS], relative Mediterranean Diet Score [rMED], and the Mediterranean Style Dietary Pattern Score [MSDPS]) that reflected different nutritional recommendations in 3,151 participants in the French SUpplémentation en Vitamines et Minéraux AntioXydants Study, found that, except for the MSDPS, the highest relative to the lowest quartiles of the scores were statistically significantly associated with lower proportional weight gain among men (range of proportional differences between the highest relative to lowest diet score quartiles among men: -0.84% – -2.17%; all $P < 0.05$), but not women[71]. In our analysis, we found that our total EC score, EC lifestyle score, and EC diet score were not associated with substantial differences in weight change. These results appear inconsistent with previous studies examining the association of diet and lifestyle scores with weight change. However, average weight change in our entire population was quite small, making it unlikely that we could detect substantial differences in mean weight change by levels of our scores or other exposures.

Our population was older than those in the above-noted previous studies, which may have contributed to our null findings. Other studies that focused on weight loss among older populations implicated multiple issues older populations face regarding weight maintenance, including disease, medication use, lower basal metabolic rate leading to lower energy intake, and social isolation[64,65]. Weight loss in older populations has also been associated with an increase in mortality. One prospective cohort study of 4,714 adults aged 65 and older from the Cardiovascular Health Study found that a 5% decrease, but not increase, in weight was associated with higher all-cause mortality risk (HR: 1.67; 95% CI: 1.29, 2.15)[72]. Another prospective cohort study of 288 frail elders receiving home support services found that involuntary weight loss of more than 1 kg in the 12 months prior to baseline was statistically significantly associated with mortality (RR: 1.76; 95% CI 1.15 – 2.71)[73]. Given that REGARDS comprises individuals older than 45 years of age, individuals in this cohort may not experience magnitudes in weight change associated with the EC score that younger populations would. More studies of associations of our evolutionary-concordance scores with weight gain in both younger and older populations are needed clarify this association.

We found that removal of no single component from our scores substantially affected our findings. However, removal of alcohol had the greatest effect on the estimated average absolute and proportional weight changes across quintiles of the total EC score, while removal of physical activity had the greatest effect on estimates of absolute and proportional BMI changes across quintiles of the total EC score. More studies in other populations in these regards are needed.

Our study has strengths and limitations. We had a large study population, long follow-up period, and a diverse cohort. To our knowledge, our study is also the first to investigate associations of evolutionary-concordance scores with weight change. First, a major limitation of our study was that the overall mean weight change (gain) in this cohort was very small and likely would have prohibited us from identifying any factors that could substantially affect long-term weight change. Second, FFQs have known limitations such as measurement error; however, in prospective studies, such error is non-differential and tends to attenuate associations, and the 110-item Block 98 Food Frequency Questionnaire we used was previously validated[51]. Third, we excluded a substantial portion of the REGARDS population, primarily due to missing exposure and outcome data. While differences in these populations may have affected results, we found only slight differences in EC score components and covariates between participants with and without follow-up weight data. We also excluded participants with medical conditions that could have outsized influences on weight change. While, this may limit the generalizability of our findings, it likely improved the internal validity of our findings. Fourth, all EC score components were self-reported, which may lead to misclassification error. However, given our prospective design, this misclassification is likely non-differential and would be expected to attenuate our results. Last, some participants may have changed their diets and lifestyles during follow-up, but we had no data on changes during follow-up;

such exposure misclassification also could have attenuated our results. We attempted to ameliorate this by excluding participants with medical conditions that may substantially change behavior and influence weight change.

In summary, while our findings did not support that lifestyle and dietary evolutionary-concordance scores, separately or combined, were associated with weight change over 10 years in the REGARDS cohort, the overall minimal mean weight change in the cohort may have prohibited identification of any exposures that would be substantially associated with weight change in a generally health population. Given the plausibility of more evolutionary-concordant diets and lifestyles possibly minimizing weight gain during adulthood, further studies among populations demonstrating more long-term weight change are needed. Such studies would benefit from more valid measures of some of the components of our evolutionary-concordance diet and lifestyle scores and longer follow-up.

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Tables

Table 1 Selected participant characteristics according to quintiles of a total evolutionary-concordance score at baseline (2003–2007) in the REGARDS cohort (n = 9,472)

Characteristics[b]	Total	**Total evolutionary-concordance score quintiles**[c]				
		1	2	3	4	5
	n = 9,472	n = 2,000 (21.1%)	n = 1,577 (16.6%)	n = 1,885 (19.9%)	n = 2,370 (25.0%)	n = 1,640 (17.3%)
Age, years	63.0 (8.4)	61.7 (8.3)	62.9 (8.3)	62.9 (8.1)	63.5 (8.4)	64.0 (8.4)
Female, %	57.7	60.7	57.0	61.5	56.9	54.4
White, %	69.2	64.9	67.5	66.4	71.2	74.8
Stroke belt region[d], %	56.1	55.0	56.9	58.5	55.8	55.5
Income < $20k, %	11.6	15.3	13.1	12.0	10.6	7.2
Married, %	65.8	59.4	65.0	66.5	67.8	70.6
Has health insurance, %	94.3	92.0	93.7	95.1	95.1	95.9
Has comorbid conditions[e], %	12.6	11.7	12.6	14.1	11.7	13.7
Take HRT (women only)[f], %	62.2	58.4	63.7	62.7	63.9	63.0
Current smoker, %	10.5	18.8	11.4	8.5	7.6	5.1
Waist circumference, cm	94.6 (14.6)	96.6 (14.4)	95.7 (15.1)	94.6 (14.7)	94.0 (14.4)	92.1 (14.0)
Body mass index, kg/m^2	29.2 (5.9)	30.0 (6.1)	29.6 (6.1)	29.6 (6.1)	28.9 (5.5)	28.0 (5.3)
Evolutionary-concordance diet score[g]	39.0 (6.1)	34.7 (5.0)	37.5 (5.7)	38.9 (5.4)	40.6 (5.5)	43.2 (5.1)
Alcohol intake, drinks/wk	2.5 (6.7)	4.7 (9.4)	2.7 (7.1)	2.0 (6.1)	1.8 (4.6)	1.0 (3.6)
Physical activity[h], times/wk	26.0 (2.3)	1.2 (1.7)	2.1 (2.0)	2.6 (2.2)	3.0 (2.2)	4.2 (2.2)
TV screen time > 2 hr/day, %	53.3	82.5	65.8	52.9	41.3	23.0
Close friends or family, no.	13.2 (12.7)	7.2 (6.3)	11.1 (10.2)	12.0 (9.9)	15.4 (13.2)	20.0 (16.6)
Dietary intakes						
Total energy, kcal/day	1,721 (696)	1,836 (727)	1,746 (712)	1,682 (689)	1,689 (689)	1,631 (641)
Total fat, %kcal	37.6	38.0	37.9	37.8	37.6	37.2
Carbohydrates, %kcal	47.8	46.6	47.5	47.9	48.1	49.1
Proteins, %kcal	14.7	14.0	14.4	14.8	15.1	15.5

Hrs Hours; *Wk* Week; *HRT* hormone replacement therapy, *REGARDS* REasons for Geographic and Racial Differences in Stroke

[a] The total evolutionary-concordance score comprises alcohol intake, physical activity, sedentary behavior, social network size, and an evolutionary-concordance diet score as described in the text; a higher score indicates higher evolutionary concordance

[b] Values presented are means (SD) or, where indicated, percentages. The following variables had missing values: income (10.2%); insurance status (0.03%)

[c] ECL score quintile ranges were as follows: quintile 1, 5–12; quintile 2, 13–14; quintile 3, 15; quintile 4, 16–17; quintile 5, 18–25

[d] Stroke belt: North Carolina, South Carolina, Arkansas, Georgia, Tennessee, Alabama, Mississippi, and Louisiana

[e] Includes cancers except non-melanoma skin cancer, end-stage renal disease, surgery or procedure on arteries, angioplasty or stenting of coronary arteries, repair of an aortic aneurism, myocardial infarction

[f] HRT use is among women only (n = 5,469). The denominators used to calculate the percent of women who used HRT within ECL score quintiles were as follows: quintile 1, n = 1,176; quintile 2, n = 957; quintile 3, n = 1,092; quintile 4, n = 1,333; quintile 5, n = 911

[g] Of a possible score range of 13 to 65, the actual score range in the study population was 17–61, with higher scores indicating greater evolutionary concordance

[h] Self-reported times per week the participant engaged in physical activity intense enough to work up a sweat

Table 2 Associations of the total evolutionary concordance score[a] with absolute and proportional weight and body mass index changes over 10 years in the REGARDS cohort (n = 4,972)

Model and variable form	**Weight change**				**BMI change**			
	Absolute mean (95% CI), kg	*P*-values	Proportional mean (%)	*P*-values	Absolute mean (95% CI)	*P*-values	Proportional mean (%)	*P*-values
Crude,[b] continuous	0.04 (-0.01, 0.10)	*0.12*	0.03 (-0.03, 0.09)	*0.28*	0.01 (-0.01, 0.03)	*0.17*	0.03 (-0.04, 0.09)	*0.41*
Crude,[b] quintiles (ranges)								
1 (5–12)	Ref.		Ref.		Ref.		Ref.	
2 (13–14)	0.22 (-0.50, 0.94)		0.22 (-0.58, 1.06)		0.14 (-0.12, 0.41)		0.46 (-0.42, 1.33)	
3 (15)	-0.03 (-1.01, 0.96)		-0.02 (-1.01, 0.96)		-0.01 (-0.34, 0.31)		-0.05 (-1.09, 1.00)	
4 (16-–7)	0.49 (-0.35, 1.31)		0.48 (-0.35, 1.31)		0.13 (-0.14, 0.40)		0.35 (-0.53, 1.23)	
5 (18–25)	0.31 (-0.59, 1.04)	*0.17*[c]	0.22 (-0.59, 1.04)	*0.37*[c]	0.11 (-0.16, 0.38)	*0.29*[c]	0.20 (-0.67, 1.06)	*0.61*[c]
Adjusted,[d] continuous	0.08 (0.02, 0.13)	*0.01*	0.08 (0.02, 0.14)	*0.01*	0.02 (0.00, 0.04)	*0.03*	0.07 (0.00, 0.13)	*0.05*
Adjusted,[d] quintiles (ranges)								
1 (5–12)	Ref.		Ref.		Ref.		Ref.	
2 (13–14)	0.50 (-0.21, 1.20)		0.60 (-0.20, 1.40)		0.23 (-0.04, 0.49)		0.76 (-0.10, 1.62)	
3 (15)	0.27 (-0.58, 1.12)		0.35 (-0.62, 1.31)		0.09 (-0.23, 0.40)		0.30 (-0.74, 1.33)	
4 (16–17)	0.85 (0.12, 1.57)		0.95 (0.13, 1.76)		0.24 (-0.03, 0.51)		0.74 (-0.74, 1.33)	
5 (18–25)	0.72 (0.00, 1.44)	*0.01*[c]	0.77 (-0.04, 1.58)	*0.01*[c]	0.23 (-0.04, 0.50)	*0.04*[c]	0.64 (-0.23, 1.51)	*0.09*[c]

BMI body mass index, *CI* Confidence interval, *Ref.* Reference, *REGARDS* REasons for Geographic and Racial Differences in Stroke

[a] The total evolutionary-concordance score comprises alcohol intake, physical activity, sedentary behavior, social network size, and a 13-component evolutionary-concordance diet score as described in the text; a higher score indicates higher evolutionary concordance

[b] From unadjusted general linear regression models

[c] *P* for trend across quintiles

[d] From multivariable-adjusted general linear regression models; adjusted for age (years), race (Black, White), sex/hormone therapy use (male, female – no hormone therapy use, female – hormone therapy use), education (less than high school, high school graduate, some college, college graduate or

above), income (<$20k, 20–34k, 35–74k, 75k+, missing), smoking at baseline (cigarettes/wk), marital status (married, single, other), health insurance (yes, no), region (stroke belt, non-stroke belt), presence of comorbidities at baseline (yes, no; defined as surgery or procedure on arteries, angioplasty or stenting of coronary arteries, repair of aortic aneurysm, myocardial infarction), total energy intake (kcal/day)

Table 3 Associations of the evolutionary concordance lifestyle score[a] with absolute and proportional weight and body mass index changes over 10 years in the REGARDS cohort (n = 4,972)

Model and variable form	Weight change				BMI change			
	Absolute mean (95% CI), kg	*P*-values	Proportional mean (%)	*P*-values	Absolute mean (95% CI)	*P*-values	Proportional mean (%)	*P*-values
Crude,[b] continuous	0.03 (-0.04, 0.09)	*0.41*	0.02 (-0.05, 0.09)	*0.65*	0.01 (-0.02, 0.03)	*0.58*	0.01 (-0.07, 0.08)	*0.88*
Crude,[b] quintiles (ranges)								
1 (5–12)	Ref.		Ref.		Ref.		Ref.	
2 (13–14)	0.16 (-0.58, 0.90)		0.18 (-0.66, 1.02)		0.05 (-0.23, 0.32)		0.16 (-0.73, 1.05)	
3 (15)	0.59 (-0.25, 1.43)		0.57 (-0.38, 1.53)		0.20 (-0.11, 0.51)		0.59 (-0.42, 1.61)	
4 (16-–7)	0.07 (-0.66, 0.81)		0.09 (-0.74, 0.93)		-0.05 (-0.33, 0.22)		-0.18 (-1.07, 0.71)	
5 (18–25)	0.40 (-0.38, 1.18)	*0.19*[c]	0.27 (-0.62, 1.16)	*0.26*[c]	0.13 (-0.16, 0.42)	*0.10*[c]	0.24 (-0.70, 1.19)	*0.19*[c]
Adjusted,[d] continuous	0.05 (-0.01, 0.11)	*0.13*	0.05 (-0.02, 0.12)	*0.18*	0.01 (-0.01, 0.04)	*0.25*	0.03 (-0.04, 0.11)	*0.41*
Adjusted,[d] quintiles (ranges)								
1 (5–12)	Ref.		Ref.		Ref.		Ref.	
2 (13–14)	0.24 (-0.49, 0.96)		0.27 (-0.55, 1.08)		0.07 (-0.20, 0.34)		0.24 (-0.64, 1.12)	
3 (15)	0.70 (-0.12, 1.53)		0.72 (-0.21, 1.65)		0.24 (-0.07, 0.55)		0.72 (-0.28, 1.72)	
4 (16–17)	0.25 (-0.47, 0.97)		0.31 (-0.50, 1.13)		0.00 (-0.27, 0.27)		0.01 (-0.87, 0.89)	
5 (18–25)	0.58 (-0.19, 1.35)	*0.10*[c]	0.50 (-0.37, 1.37)	*0.11*[c]	0.17 (-0.11, 0.46)	*0.06*[c]	0.42 (-0.52, 1.35)	*0.11*[c]

BMI body mass index, *CI* Confidence interval, *Ref.* Reference, *REGARDS* REasons for Geographic and Racial Differences in Stroke

[a] The evolutionary-concordance lifestyle score comprises alcohol intake, physical activity, sedentary behavior, and social network size as described in the text; a higher score indicates higher evolutionary concordance

[b] From unadjusted general linear regression models

[c] *P* for trend across quintiles

[d] From multivariable-adjusted general linear regression models; adjusted for age (years), race (Black, White), sex/hormone therapy use (male, female – no hormone therapy use, female – hormone therapy use), education (less than high school, high school graduate, some college, college graduate or

above), income (<$20k, 20–34k, 35–74k, 75k+, missing), smoking at baseline (cigarettes/wk), marital status (married, single, other), health insurance (yes, no), region (stroke belt, non-stroke belt), presence of comorbidities at baseline (yes, no; defined as surgery or procedure on arteries, angioplasty or stenting of coronary arteries, repair of aortic aneurysm, myocardial infarction), total energy intake (kcal/day)

Table 4 Associations of the evolutionary concordance diet score[a] with absolute and proportional weight and body mass index changes over 10 years in the REGARDS cohort (n = 4,972)

Model and variable form	**Weight change**				**BMI change**			
	Absolute mean (95% CI), kg	*P*-values	Proportional mean (%)	*P*-values	Absolute mean (95% CI)	*P*-values	Proportional mean (%)	*P*-values
Crude,[b] continuous	0.12 (0.00, 0.25)	*0.05*	0.11 (-0.03, 0.26)	*0.11*	0.05 (0.00, 0.09)	*0.04*	0.12 (-0.03, 0.27)	*0.11*
Crude,[b] quintiles (ranges)								
1 (5–12)	Ref.		Ref.		Ref.		Ref.	
2 (13–14)	0.16 (-0.58, 0.90)		0.18 (-0.66, 1.02)		0.05 (-0.23, 0.32)		0.16 (-0.73, 1.05)	
3 (15)	0.59 (-0.25, 1.43)		0.57 (-0.38, 1.53)		0.20 (-0.11, 0.51)		0.59 (-0.42, 1.61)	
4 (16–7)	0.07 (-0.66, 0.81)		0.09 (-0.74, 0.93)		-0.05 (-0.33, 0.22)		-0.18 (-1.07, 0.71)	
5 (18–25)	0.40 (-0.38, 1.18)	*0.04*[c]	0.27 (-0.62, 1.16)	*0.09*[c]	0.13 (-0.16, 0.42)	*0.02*[c]	0.24 (-0.70, 1.19)	*0.07*[c]
Adjusted,[d] continuous	0.23 (0.10, 0.35)	*0.001*	0.26 (0.12, 0.41)	*0.001*	0.08 (0.03, 0.13)	*0.001*	0.24 (0.09, 0.40)	*0.002*
Adjusted,[d] quintiles (ranges)								
1 (5–12)	Ref.		Ref.		Ref.		Ref.	
2 (13–14)	0.47 (-0.27, 1.21)		0.58 (-0.25, 1.42)		0.27 (-0.01, 0.55)		0.79 (-0.11, 1.69)	
3 (15)	0.64 (-0.13, 1.42)		0.68 (-0.20, 1.56)		0.28 (-0.01, 0.57)		0.74 (-0.20, 1.68)	
4 (16–17)	0.57 (-0.19, 1.33)		0.74 (-0.13, 1.59)		0.22 (-0.07, 0.50)		0.66 (-0.26, 1.58)	
5 (18–25)	1.24 (0.45, 2.03)	*0.001*[c]	1.41 (0.52, 2.30)	*0.001*[c]	0.49 (0.20, 0.79)	*0.001*[c]	1.47 (0.51, 2.43)	*0.001*[c]

BMI body mass index, *CI* Confidence interval, *Ref.* Reference, *REGARDS* REasons for Geographic and Racial Differences in Stroke

[a] The evolutionary-concordance diet score comprises vegetables, fruits, lean meats, fish, nuts, red and processed meats, dairy, grains and starches, baked goods, sugar-sweetened beverages (grams), sodium and calcium (mg), and a fruit and vegetable diversity score, calculated from the sum of the total number of responses on the fruit and vegetable sections of the FFQ that indicated the participant ate > 1 – 3 servings of a given line-item per month.; a higher score indicates higher evolutionary concordance

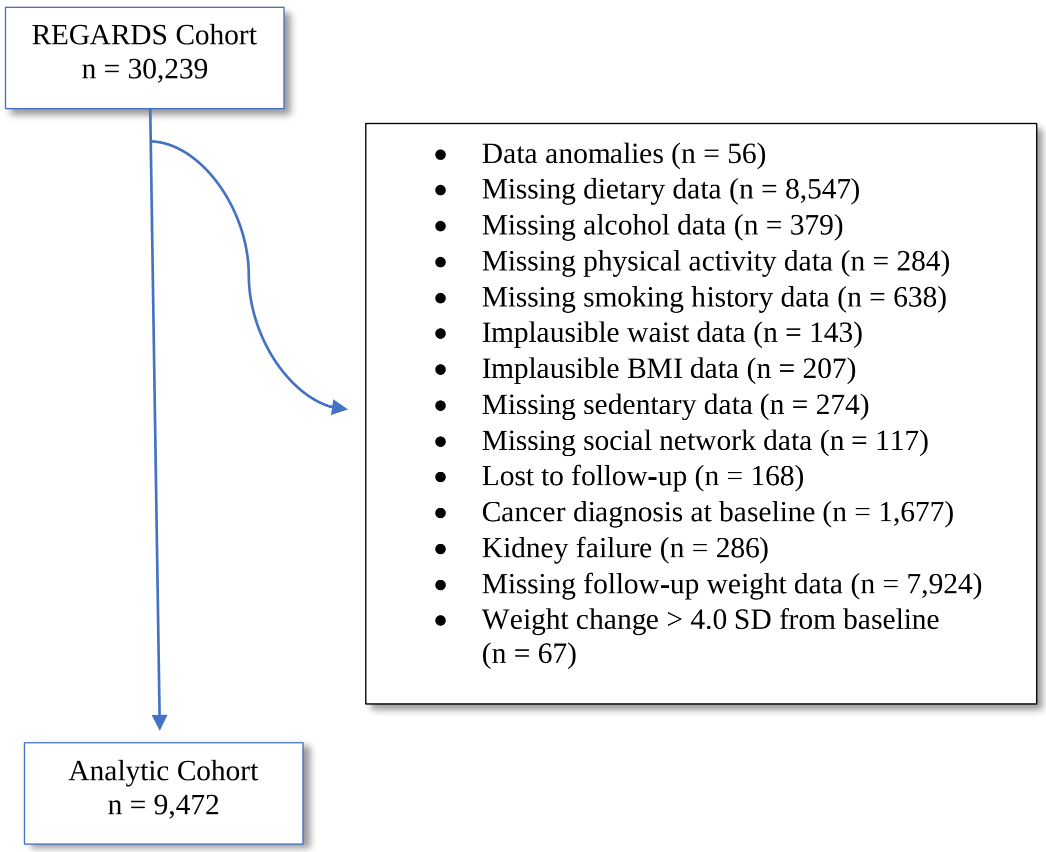
[b] From unadjusted general linear regression models

[c] *P* for trend across quintiles

[d] From multivariable-adjusted general linear regression models; adjusted for age (years), race (Black, White), sex/hormone therapy use (male, female – no hormone therapy use, female – hormone therapy use), education (less than high school, high school graduate, some college, college graduate or above), income (<$20k, 20–34k, 35–74k, 75k+, missing), smoking at baseline (cigarettes/wk), marital status (married, single, other), health insurance (yes, no), region (stroke belt, non-stroke belt), presence of comorbidities at baseline (yes, no; defined as surgery or procedure on arteries, angioplasty or stenting of coronary arteries, repair of aortic aneurysm, myocardial infarction), total energy intake (kcal/day)

Figures

Figure 1 Exclusion flow chart among the REasons for Geographic and Racial Differences in Stroke (REGARDS) cohort



Appendix

Supplemental Table 1 Differences in baseline participant characteristics between participants with and without follow-up weight data in the REGARDS Cohort (n = 30,183)

Population characteristics[a]	**Participants without follow-up weight data** n = 15,818	**Participants with follow-up weight data** n = 14,365	***P-value***
Age, years	66.3 (10.1)	63.2 (8.4)	*0.01*
Female, %	54.2	56.1	*0.01*
White, %	54.3	63.2	*0.01*
Stroke belt region[b], %	55.4	55.6	*0.67*
Income, %			*0.01*
Less than $20k	22.9	12.9	
$20k – $34k	26.0	22.2	
$35k – $74k	25.9	33.5	
$75k and above	11.4	20.6	
Married, %	53.8	64.1	*0.01*
Has health insurance, %	92.7	94.0	*0.01*
Has comorbid conditions[c], %	31.0	20.0	*0.01*
Take HRT (women only)[d], %	51.1	59.3	*0.01*
Smoking status, %			*0.01*
Never	41.8	49.0	
Current	17.9	11.0	
Past	40.3	40.0	
Waist circumference, cm	97.0 (16.1)	95.3 (15.2)	*0.01*
BMI, kg/m^2	29.3 (6.4)	29.3 (6.0)	*0.48*
Alcohol intake, drinks/wk	2.0 (6.2)	2.3 (6.4)	*0.01*
Physical activity[e], times/wk	2.33 (2.4)	2.55 (2.3)	*0.01*
TV screen time > 2 hr/day, %	61.5	54.4	*0.01*
Close friends or family, no.	13.1 (15.4)	13.4 (15.5)	*0.01*
Dietary intakes			
Total energy, kcal/day	1,695 (728)	1,722 (698)	*0.01*
Total fat, %kcal	37.1 (8.0)	37.6 (7.7)	*0.01*
Carbohydrates, %kcal	48.9 (9.5)	47.9 (9.2)	*0.01*
Protein, %kcal	14.4 (3.2)	14.7 (3.1)	*0.01*

Hrs Hours; *Wk* Week; *HRT* hormone replacement therapy, *REGARDS* Reasons for Geographic and Racial Differences in Stroke

[a] Values presented are means (SD) or percentages. The following variables had missing values: region (0.003%); income (12.4%); insurance (0.1%); smoking status (0.4%); waist circumference (0.6%); BMI (0.7%); total energy intake (28.3%); alcohol intake (2.0%); physical activity (1.5%); TV screen time (21.5%); # close friends and family (0.9%)

[b] Stroke belt: North Carolina, South Carolina, Arkansas, Georgia, Tennessee, Alabama, Mississippi, and Louisiana

[c] Includes surgery or procedure on arteries, angioplasty or stenting of coronary arteries, repair of an aortic aneurism, myocardial infarction

[d] HRT use is described among women only (n=16,632). The denominators used to calculate the percent of women who used HRT within each group were: participants without follow-up weight and BMI data, n=8,579; participants with follow-up weight and BMI data, n=8,053

[e] Self-reported times per week the participant engaged in physical activity intense enough to work up a sweat

Supplemental Table 2 Associations of the total evolutionary concordance score[a] with absolute and proportional waist circumference changes over 10 years in the REGARDS cohort (n = 9,472)

Model and variable form	**Waist circumference changes**			
	Absolute mean (95% CI), cm	*P-value*	Proportional mean (%)	*P-value*
Crude,[b] continuous	0.06 (-0.01, 0.13)	*0.10*	0.08 (0.00, 0.15)	*0.05*
Crude,[b] quintiles (ranges)				
1 (5–12)	Ref.		Ref.	
2 (13–14)	0.31 (-0.62, 1.24)		0.43 (-0.58, 1.43)	
3 (15)	0.10 (-1.02, 1.22)		0.08 (-1.13, 1.29)	
4 (16-–7)	0.39 (-0.55, 1.33)		0.51 (-0.51, 1.53)	
5 (18–25)	0.37 (-1.30, 0.55)	*0.27*[c]	0.52 (-1.53, 0.48)	*0.16*[c]
Adjusted,[d] continuous	0.09 (0.01, 0.16)	*0.02*	0.10 (0.02, 0.18)	*0.01*
Adjusted,[d] quintiles (ranges)				
1 (5–12)	Ref.		Ref.	
2 (13–14)	0.51 (-0.42, 1.43)		0.64 (-0.37, 1.64)	
3 (15)	0.28 (-0.84, 1.39)		0.24 (-0.96, 1.45)	
4 (16–17)	0.62 (-0.32, 1.57)		0.75 (-0.28, 1.77)	
5 (18–25)	0.66 (-0.28, 1.60)	*0.06*[c]	0.82 (-0.19, 1.84)	*0.03*[c]

CI Confidence interval, *Ref.* Reference, *REGARDS* REasons for Geographic and Racial Differences in Stroke

[a] The total evolutionary-concordance score comprises alcohol intake, physical activity, sedentary behavior, social network size, and an evolutionary-concordance diet score as described in the text; a higher score indicates higher evolutionary concordance

[b] From unadjusted general linear regression models

[c] *P* for trend across quintiles

[d] From multivariable-adjusted general linear regression models; adjusted for age (years), race (Black, White), sex/hormone therapy use (male, female – no hormone therapy use, female – hormone therapy use), education (less than high school, high school graduate, some college, college graduate or above), income (<$20k, 20–34k, 35–74k, 75k+, missing), smoking at baseline (cigarettes/wk), marital status (married, single, other), health insurance (yes, no), region (stroke belt, non-stroke belt), presence of comorbidities at baseline (yes, no; defined as surgery or procedure on arteries, angioplasty or stenting of coronary arteries, repair of aortic aneurysm, myocardial infarction), total energy intake (kcal/day)

Supplemental Table 3 Multivariable-adjusted[a] mean absolute and proportional weight and BMI changes across total evolutionary-concordance score[b] quintiles, stratified by baseline smoking status in the REGARDS cohort (*n* = 9,472)

Baseline smoking status	**Total EC score quintiles (quintile ranges)**					
	1 (5–12)	**2** (13–14)	**3** (15)	**4** (16–17)	**5** (18–25)	P_{trend}[c]
Never[d]						
Absolute weight change, kg	Ref.	0.55 (-0.46, 1.56)	0.04 (-1.14, 1.22)	0.68 (-0.32, 1.69)	0.54 (-0.44, 1.52)	*0.15*
Proportional weight change, %	Ref.	0.55 (-0.61, 1.71)	-0.01 (-1.37, .34)	0.69 (-0.46, 1.85)	0.47 (-0.65, 1.60)	*0.28*
Absolute BMI change	Ref.	0.18 (-0.20, 0.57)	-0.08 (0.53, 0.38)	0.09 (0.30, 0.47)	0.13 (-0.25, 0.50)	*0.50*
Proportional BMI change, %	Ref.	0.55 (0.70, 1.80)	-0.34 (-1.81, 1.12)	0.15 (-1.10, 1.40)	0.22 (-1.00, 1.43)	*0.84*
Current						
Absolute weight change, kg	Ref.	1.02 (-1.14, 3.18)	1.12 (-1.91, 4.14)	1.80 (-0.74, 4.33)	0.40 (-2.49, 3.24)	*0.21*
Proportional weight change	Ref.	1.19 (1.39, 3.78)	1.46 (-2.16, 5.07)	2.06 (-0.96, 5.09)	0.50 (-2.90, 3.90)	*0.21*
Absolute BMI change	Ref.	0.46 (-0.33, 1.24)	0.44 (-0.66, 1.53)	0.60 (0.33, 1.51)	0.17 (0.87, 1.19)	*0.21*
Proportional BMI change	Ref.	1.48 (-1.21, 4.17)	1.89 (-1.87, 5.66)	2.04 (-1.11, 5.19)	0.49 (-3.05, 4.03)	*0.21*
Former						
Absolute weight change, kg	Ref.	0.05 (-1.09, 1.19)	0.12 (-1.24, 1.49)	0.58 (-0.59, 1.75)	0.66 (-0.52, 1.84)	*0.08*
Proportional weight change	Ref.	0.19 (-1.05, 1.43)	0.23 (-1.25, 1.71)	0.70 (-0.57, 1.97)	0.79 (-0.49, 2.07)	*0.06*
Absolute BMI change	Ref.	0.12 (-0.30, 0.54)	0.11 (-0.39, 0.61)	0.25 (-0.18, 0.68)	0.25 (-0.19, 0.68)	*0.09*
Proportional BMI change, %	Ref.	0.46 (-0.87, 1.80)	0.37 (-1.23, 1.97)	0.84 (-0.53, 2.21)	0.76 (-0.62, 2.14)	*0.10*

BMI body mass index, *EC* Evolutionary-concordance, *Ref* Reference, *REGARDS* REasons for Geographic and Racial Differences in Stroke

[a] From multivariable-adjusted general linear regression models; adjusted for age (years), race (Black, White), sex/hormone therapy use (male, female – no hormone therapy use, female – hormone therapy use), education (less than high school, high school graduate, some college, college graduate or above), income (<$20k, 20–34k, 35–74k, 75k+, missing), marital status (married, single, other), health insurance (yes, no), region (stroke belt, non-stroke belt), presence of comorbidities at baseline (yes, no; defined as surgery or procedure on arteries, angioplasty or stenting of coronary arteries, repair of aortic aneurysm, myocardial infarction), total energy intake (kcal/day)

[b] The total evolutionary-concordance score comprises alcohol intake, physical activity, sedentary behavior, social network size, and an evolutionary-concordance diet score as described in the text; a higher score indicates higher evolutionary concordance

[c] P_{trend} calculated by assigning the median score of each total EC score quintile to its corresponding quintile and treating this quintile exposure as a continuous variable in the multivariable-adjusted general linear model

[d] Defined as reporting having smoked less than 100 cigarettes in participant's lifetime

Supplemental Table 4 Multivariable-adjusted[a] mean absolute and proportional weight and BMI changes across total evolutionary-concordance score[b] quintiles, stratified by baseline age category in the REGARDS cohort (*n* = 9,472)

Age category	Total EC score quintiles (quintile ranges)					
	1 (5–12)	**2** (13–14)	**3** (15)	**4** (16–17)	**5** (18–25)	$\boldsymbol{P}_{\mathbf{trend}}$[c]
45–60 yrs.						
Absolute weight change, kg	Ref.	0.45 (-0.69, 1.59)	0.16 (-1.23, 1.55)	0.52 (-0.68, 1.71)	0.09 (-1.10, 1.29)	*0.75*
Proportional weight change, %	Ref.	0.56 (-0.69, 1.81)	0.30 (-1.22, 1.83)	0.55 (-0.76, 1.86)	0.02 (-1.29, 1.33)	*0.89*
Absolute BMI change	Ref.	0.25 (-0.17, 0.68)	0.11 (0.40, 0.63)	0.10 (-0.34, 0.54)	0.03 (-0.42, 0.47)	*0.95*
Proportional BMI change, %	Ref.	0.79 (-0.54, 2.13)	0.51 (-1.12, 2.13)	0.41 (-0.98, 1.81)	-0.04 (-1.44, 1.36)	*0.09*
60–70 yrs.						
Absolute weight change, kg	Ref.	0.55 (-0.57, 1.67)	0.15 (-1.18, 1.48)	0.82 (-0.32, 1.95)	0.96 (-0.17, 2.10)	*0.02*
Proportional weight change, %	Ref.	0.70 (-0.56, 1.97)	0.12 (-1.38, 1.62)	0.95 (-0.34, 2.23)	1.11 (-0.17, 2.39)	*0.02*
Absolute BMI change	Ref.	0.18 (-0.23, 0.60)	0.08 (-0.41, 0.57)	0.27 (-0.15, 0.69)	0.30 (-0.12, 0.72)	*0.05*
Proportional BMI change, %	Ref.	0.68 (-0.67, 2.04)	0.13 (-1.47, 1.73)	0.80 (-0.57, 2.18)	0.92 (-0.45, 2.29)	*0.07*
>70 yrs.						
Absolute weight change, kg	Ref.	-0.06 (-1.61, 1.48)	0.39 (-1.49, 2.27)	0.93 (-0.61, 2.47)	0.73 (-0.76, 2.21)	*0.09*
Proportional weight change, %	Ref.	-0.22 (-2.11, 1.67)	0.40 (-1.90, 2.69)	0.94 (-0.94, 2.82)	0.64 (-1.18, 2.46)	*0.19*
Absolute BMI change	Ref.	0.10 (-0.51, 0.70)	-0.08 (-0.82, 0.65)	0.24 (-0.36, 0.84)	0.23 (-0.35, 0.81)	*0.22*
Proportional BMI change, %	Ref.	0.24 (-1.84, 2.33)	-0.28 (-2.81, 2.25)	0.56 (-1.51, 2.63)	0.55 (-1.46, 2.55)	*0.40*

BMI body mass index, *EC* Evolutionary-concordance, *Ref* Reference, *REGARDS* REasons for Geographic and Racial Differences in Stroke

[a] From multivariable-adjusted general linear regression models; adjusted for age (years), race (Black, White), sex/hormone therapy use (male, female – no hormone therapy use, female – hormone therapy use), education (less than high school, high school graduate, some college, college graduate or above), income (<$20k, 20–34k, 35–74k, 75k+, missing), marital status (married, single, other), health insurance (yes, no), region (stroke belt, non-stroke belt), presence of comorbidities at baseline (yes, no; defined as surgery or procedure on arteries, angioplasty or stenting of coronary arteries, repair of aortic aneurysm, myocardial infarction), total energy intake (kcal/day)

[b] The total evolutionary-concordance score comprises alcohol intake, physical activity, sedentary behavior, social network size, and an evolutionary-concordance diet score as described in the text; a higher score indicates higher evolutionary concordance

[c] P_{trend} calculated by assigning the median score of each total EC score quintile to its corresponding quintile and treating this quintile exposure as a continuous variable in the multivariable-adjusted general linear model

Supplemental Table 5 Multivariable-adjusted[a] mean absolute and proportional weight and BMI changes across total evolutionary-concordance score[b] quintiles, stratified by race in the REGARDS cohort (n = 9,472)

Race	Total EC score quintiles (quintile ranges)					
	1 (5–12)	**2** (13–14)	**3** (15)	**4** (16–17)	**5** (18–25)	P_{trend}[c]
White						
Absolute weight change, kg	Ref.	0.23 (-0.62, 1.07)	0.16 (-0.86, 1.18)	0.67 (-0.19, 1.52)	0.50 (-0.34, 1.33)	*0.07*
Proportional weight change, %	Ref.	0.39 (-0.58, 1.37)	0.23 (-0.94, 1.41)	0.73 (-0.25, 1.72)	0.49 (-0.47, 1.46)	*0.14*
Absolute BMI change	Ref.	0.15 (0.16, 0.46)	0.07 (-0.30, 0.45)	0.18 (-0.14, 0.49)	0.18 (-0.13, 0.49)	*0.12*
Proportional BMI change, %	Ref.	0.56 (-0.49, 1.61)	0.25 (1.01, 1.52)	0.55 (-0.51, 1.61)	0.49 (-0.54, 1.53)	*0.24*
Black						
Absolute weight change, kg	Ref.	0.96 (-0.33, 2.28)	0.38 (-1.18, 1.94)	1.14 (-0.23, 2.52)	1.10 (-0.32, 2.51)	*0.05*
Proportional weight change, %	Ref.	0.93 (-0.47, 2.34)	0.46 (-1.23, 2.14)	1.32 (-0.17, 2.80)	1.30 (-0.23, 2.83)	*0.03*
Absolute BMI change	Ref.	0.35 (-0.15, 0.85)	0.07 (-0.53, 0.67)	0.34 (-0.53, 0.67)	0.28 (-0.26, 0.83)	*0.20*
Proportional BMI change, %	Ref.	1.05 (-0.46, 2.56)	0.25 (-1.55, 2.07)	1.06 (-0.54, 2.65)	0.82 (-0.82, 2.46)	*0.20*

BMI body mass index, *EC* Evolutionary-concordance, *Ref* Reference, *REGARDS* REasons for Geographic and Racial Differences in Stroke

[a] From multivariable-adjusted general linear regression models; adjusted for age (years), sex/hormone therapy use (male, female – no hormone therapy use, female – hormone therapy use), education (less than high school, high school graduate, some college, college graduate or above), income (<$20k, 20–34k, 35–74k, 75k+, missing), marital status (married, single, other), health insurance (yes, no), region (stroke belt, non-stroke belt), presence of comorbidities at baseline (yes, no; defined as surgery or procedure on arteries, angioplasty or stenting of coronary arteries, repair of aortic aneurysm, myocardial infarction), total energy intake (kcal/day)

[b] The total evolutionary-concordance score comprises alcohol intake, physical activity, sedentary behavior, social network size, and an evolutionary-concordance diet score as described in the text; a higher score indicates higher evolutionary concordance

[c] P_{trend} calculated by assigning the median score of each total EC score quintile to its corresponding quintile and treating this quintile exposure as a continuous variable in the multivariable-adjusted general linear model

Supplemental Table 6 Multivariable-adjusted[a] mean absolute and proportional weight and BMI changes across total evolutionary-concordance score[b] quintiles, stratified by sex and hormone replacement therapy (HRT) use in the REGARDS cohort (*n* = 9,472)

Sex and HRT use	Total EC score quintiles (quintile ranges)					
	1 (5–12)	**2** (13–14)	**3** (15)	**4** (16–17)	**5** (18–25)	P_{trend}[c]
Male (no HRT use)						
Absolute weight change, kg	Ref.	0.21 (-1.05, 1.09)	-0.11 (-1.43, 1.21)	0.28 (-0.81, 1.37)	0.26 (-0.81, 1.33)	*0.43*
Proportional weight change, %	Ref.	0.13 (-0.98, 1.24)	-0.11 (-1.49, 1.26)	0.26 (-0.88, 1.40)	0.28 (-0.83, 1.40)	*0.46*
Absolute BMI change	Ref.	0.10 (-0.26, 0.46)	-0.14 (-0.59, 0.31)	0.05 (-0.32, 0.42)	0.04 (-0.32, 0.40)	*0.83*
Proportional BMI change, %	Ref.	0.42 (-0.80, 1.63)	-0.53 (-2.03, 0.98)	0.19 (-1.06, 1.43)	0.09 (-1.12, 1.31)	*0.95*
Female (no HRT use)						
Absolute weight change, kg	Ref.	1.08 (-0.53, 2.68)	0.07 (-1.82, 1.96)	1.54 (-0.10, 3.18)	0.63 (-1.00, 2.27)	*0.19*
Proportional weight change, %	Ref.	1.42 (-0.43, 3.27)	0.44 (-1.74, 2.62)	1.92 (0.03, 3.82)	0.56 (-1.33, 2.45)	*0.28*
Absolute BMI change	Ref.	0.44 (-0.21, 1.08)	0.16 (-0.61, 0.92)	0.47 (-0.20, 1.13)	0.16 (-0.50, 0.82)	*0.43*
Proportional BMI change, %	Ref.	1.60 (-0.42, 3.62)	0.96 (-1.42, 3.35)	1.57 (0.50, 3.64)	0.39 (-1.67, 2.46)	*0.50*
Female (HRT use)						
Absolute weight change, kg	Ref.	0.50 (-0.67, 1.67)	0.64 (-0.73, 2.01)	0.86 (-0.33, 2.05)	1.00 (-0.19, 2.21)	*0.02*
Proportional weight change, %	Ref.	0.42 (-0.98, 1.83)	0.61 (-1.04, 2.26)	0.92 (-0.51, 2.36)	1.09 (-0.35, 2.54)	*0.03*
Absolute BMI change	Ref.	0.19 (-0.27, 0.64)	0.23 (-0.30, 0.77)	0.23 (-0.24, 0.70)	0.37 (-0.09, 0.84)	*0.03*
Proportional BMI change, %	Ref.	0.43 (-1.05, 1.91)	0.60 (-1.14, 2.34)	0.62 (-0.89, 2.13)	1.06 (-0.46, 2.58)	*0.06*

BMI body mass index, *EC* Evolutionary-concordance, *HRT* Hormone Replacement Therapy, *Ref* Reference, *REGARDS* REasons for Geographic and Racial Differences in Stroke

[a] From multivariable-adjusted general linear regression models; adjusted for age (years), race (Black, White), education (less than high school, high school graduate, some college, college graduate or above), income (<$20k, 20–34k, 35–74k, 75k+, missing), marital status (married, single, other), health insurance (yes, no), region (stroke belt, non-stroke belt), presence of comorbidities at baseline (yes, no; defined as surgery or procedure on arteries, angioplasty or stenting of coronary arteries, repair of aortic aneurysm, myocardial infarction), total energy intake (kcal/day)

[b] The total evolutionary-concordance score comprises alcohol intake, physical activity, sedentary behavior, social network size, and an evolutionary-concordance diet score as described in the text; a higher score indicates higher evolutionary concordance

[c] P_{trend} calculated by assigning the median score of each total EC score quintile to its corresponding quintile and treating this quintile exposure as a continuous variable in the multivariable-adjusted general linear model

Supplemental Table 7 Multivariable-adjusted[a] mean absolute and proportional weight and BMI changes across total evolutionary-concordance score[b] quintiles, stratified by baseline comorbidity status[c] in the REGARDS cohort (*n* = 9,472)

Baseline comorbidity status	**Total EC score quintiles (quintile ranges)**					
	1 (5–12)	**2** (13–14)	**3** (15)	**4** (16–17)	**5** (18–25)	P_{trend}[d]
No comorbidities						
Absolute weight change, kg	Ref.	0.54 (-0.21, 1.30)	0.29 (-0.62, 1.20)	0.79 (0.03, 1.56)	0.60 (-0.16, 1.37)	*0.03*
Proportional weight change, %	Ref.	0.60 (-0.25, 1.45)	0.28 (-0.75, 1.32)	0.88 (0.12, 1.75)	0.61 (-0.26, 1.45)	*0.05*
Absolute BMI change	Ref.	0.26 (-0.02, 0.55)	0.12 (-0.04, 0.54)	0.25 (-0.04, (0.54)	0.20 (-0.09, 0.49)	*0.08*
Proportional BMI change, %	Ref.	0.84 (-0.07, 1.76)	0.36 (-0.75, 1.47)	0.77 (-0.17, 1.70)	0.53 (-0.40, 1.46)	*0.16*
With comorbidities						
Absolute weight change, kg	Ref.	0.09 (-2.03, 2.21)	0.08 (-2.38, 2.54)	1.11 (-1.09, 3.31)	1.11 (-1.02, 3.27)	*0.10*
Proportional weight change, %	Ref.	0.55 (-1.79, 2.89)	0.71 (-2.01, 3.42)	1.30 (-1.13, 3.73)	1.45 (0.90, 3.81)	*0.07*
Absolute BMI change	Ref.	-0.06 (-0.82, 0.70)	-0.17 (-1.04, 0.71)	0.13 (-0.66, 0.92)	0.28 (-0.48, 1.04)	*0.24*
Proportional BMI change, %	Ref.	0.09 (-2.38, 2.57)	-0.18 (-3.05, .69)	0.45 (-2.12, 3.02)	0.95 (-1.54, 3.43)	*0.26*

BMI body mass index, *EC* Evolutionary-concordance, *Ref* Reference, *REGARDS* REasons for Geographic and Racial Differences in Stroke

[a] From multivariable-adjusted general linear regression models; adjusted for age (years), race (Black, White), sex/hormone therapy use (male, female – no hormone therapy use, female – hormone therapy use), education (less than high school, high school graduate, some college, college graduate or above), income (<$20k, 20–34k, 35–74k, 75k+, missing), marital status (married, single, other), health insurance (yes, no), region (stroke belt, non-stroke belt), total energy intake (kcal/day)

[b] The total evolutionary-concordance score comprises alcohol intake, physical activity, sedentary behavior, social network size, and an evolutionary-concordance diet score as described in the text; a higher score indicates higher evolutionary concordance

[c] Defined as baseline history of surgery or procedure on arteries, angioplasty or stenting of coronary arteries, repair of aortic aneurysm, or myocardial infarction (yes/no)

[d] P_{trend} calculated by assigning the median score of each total EC score quintile to its corresponding quintile and treating this quintile exposure as a continuous variable in the multivariable-adjusted general linear model

Supplemental Table 8 Multivariable-adjusted[a] mean absolute and proportional weight and BMI changes over 10 years among those in the highest relative to the lowest quintiles of the total evolutionary-concordance score,[b] overall and after removing and replacing each of its five components one at a time; REGARDS cohort (n = 9,472)

EC score variant removed	**Absolute weight change**	**Proportional weight change**	**Absolute BMI change**	**Proportional BMI change**
	Highest to lowest quintile difference (95% CI)	Highest to lowest quintile difference (95% CI)	Highest to lowest quintile difference (95% CI)	Highest to lowest quintile difference (95% CI)
None[b]	0.72 (0.00, 1.44)	0.77 (-0.04, 1.58)	0.23 (-0.04, 0.50)	0.64 (-0.23, 1.51)
EC diet score[c]	0.48 (-0.29, 1.26)	0.39 (-0.49, 1.26)	0.14 (-0.15, 0.43)	0.30 (-0.63, 1.24)
Alcohol intake	1.29 (0.56, 2.03)	1.33 (0.50, 2.16)	0.39 (0.12, 0.67)	1.11 (0.22, 2.00)
Physical activity	0.36 (-0.43, 1.14)	0.45 (-0.43, 1.34)	0.12 (-0.18, 0.41)	0.36 (-0.60, 1.31)
Sedentary behavior	0.73 (-0.05, 1.52)	0.88 (0.01, 1.76)	0.24 (-0.05, 0.54)	0.70 (-0.26, 1.65)
Social network size	0.84 (0.07, 1.62)	0.90 (0.03, 1.78)	0.31 -0.02, 0.60)	0.94 (0.00, 1.88)

EC Evolutionary-concordance, *Ref* Reference, *REGARDS* REasons for Geographic and Racial Differences in Stroke

[a] From multivariable general linear models, adjusted for age (years), race (black, white), sex/hormone therapy use (male, female – no hormone therapy use, female – hormone therapy use), education (less than high school, high school graduate, some college, college graduate or above); income (<$20k, 20-34k, 35-74k, 75k+, missing), smoking at baseline (cigarettes/wk), marital status (married, single, other), health insurance (yes, no), region (stroke belt, non-stroke belt), presence of comorbidities at baseline (yes, no; defined as cancer, ESRD, surgery or procedure on arteries, angioplasty or stenting of coronary arteries, repair of aortic aneurysm, myocardial infarction), total energy intake kcal/day), and the respective removed component

[b] The total evolutionary-concordance score comprises alcohol intake, physical activity, sedentary behavior, social network size, and an evolutionary-concordance diet score as described in the text; a higher score indicates higher evolutionary concordance

[c] The 13-component EC score is described in the text; a higher score indicates higher evolutionary concordance