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Association of an evolutionary-concordance lifestyle pattern score with incident CVD among Black and White men and women

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Abstract

Dietary and lifestyle evolutionary discordance is hypothesised to play a role in the aetiology of CVD, including CHD and stroke. We aimed to investigate associations of a previously reported, total (dietary plus lifestyle) evolutionary-concordance (EC) pattern score with incident CVD, CHD and stroke. We used multivariable Cox proportional hazards regression to investigate associations of the EC score with CVD, CHD and stroke incidence among USA Black and White men and women ≥45 years old in the prospective REasons for Geographic and Racial Differences in Stroke study (2003–2017). The EC score comprised seven equally weighted components: a previously reported dietary EC score (using Block 98 FFQ data) and six lifestyle characteristics (alcohol intake, physical activity, sedentary behaviour, waist circumference, smoking history and social network size). A higher score indicates a more evolutionary-concordant dietary/lifestyle pattern. Of the 15 467 participants in the analytic cohort without a CVD diagnosis at baseline, 1563 were diagnosed with CVD (967 with CHD and 596 with stroke) during follow-up (median 11·0 years). Among participants in the highest relative to the lowest EC score quintile, the multivariable-adjusted hazards ratios and their 95 % CI for CVD, CHD and stroke were, respectively, 0·73 (0·62, 0·86; $P_{trend} < 0·001$), 0·72 (0·59, 0·89; $P_{trend} < 0·001$) and 0·76 (0·59, 0·98; $P_{trend} = 0·01$). The results were similar by sex and race. Our findings support that a more evolutionary-concordant diet and lifestyle pattern may be associated with lower risk of CVD, CHD and stroke.

Keywords: **Evolutionary-concordance lifestyle: Evolutionary-concordance diet: Diets: Lifestyles: CVD risk: Prospective cohort studies**

CVD is the leading cause of death and a major cause of disability globally[1]. Evidence suggests that a large portion of the CVD burden is attributable to modifiable factors, such as smoking, unhealthy diets, excess adiposity and physical inactivity[2]. One potential explanation for this link is through the evolutionary discordance hypothesis, which posits that modern departure from the diet and lifestyle patterns of our hunter-gatherer ancestors may be a primary contributor to chronic disease risk[3]. This hypothesis led to an increasing popularity of the Paleolithic diet pattern (hereafter referred to as the evolutionary-concordant diet pattern), estimated from archeological and paleontological evidence and studies of extant hunter-gatherer populations and characterised by high intakes of fruits, vegetables, lean meats and nuts and low intakes of grains, dairy products, refined fats and sugars and salt[3,4]. Other lifestyle behaviours that are more evolutionary concordant include high levels of physical activity, low levels of sedentary behaviour, limited alcohol consumption, energy balances that limit excess adiposity, not using tobacco and high social connectiveness[4–6].

Evidence from clinical trials suggests that a more evolutionary-concordant diet pattern may be associated with more favourable CVD risk factors and biomarkers[7,8]. Also, observational studies suggest that a more evolutionary-concordant diet pattern may be inversely associated with ageing-related diseases[9,10] and CVD mortality[11,12]. Multiple dietary and lifestyle behaviours coexist and may interact to influence health. Thus, evolutionary-concordance (EC) scores (comprising diet and other lifestyle factors) were developed and reported to reflect the relative closeness of someone's dietary and lifestyle patterns to evolutionary-concordant patterns[10,12,13].

Abbreviations: EC, evolutionary-concordance; HR, hazards ratios; REGARDS, REasons for Geographic and Racial Differences in Stroke.

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EC scores were previously reported to be associated with incident colorectal cancer[10] and all-cause and cause-specific mortality[12,13]. However, only two studies (a prospective study among Spanish adults and a cross-sectional study among Australian adults) reported an association of a dietary EC score with CVD[14,15], and no study has reported an association of a lifestyle EC score, with or without a dietary component, with incident CVD.

Therefore, in the present study, we investigated associations of a previously reported, seven-component EC score[13] (comprising an EC diet score, alcohol consumption, physical activity, sedentary behaviour, waist circumference, tobacco smoking history and social network size) with incident CVD, CHD and stroke, in a large, prospective cohort of White and Black American men and women. We hypothesised that more evolutionary-concordant diet and lifestyle patterns would be associated with lower CVD, CHD and stroke risk.

Methods

Study population and data collection

Details of the REasons for Geographic and Racial Differences in Stroke REGARDS) prospective cohort study were previously described[16]. Briefly, the REGARDS cohort was enrolled January 2003–October 2007 using a stratified random sampling design within geographic-race-sex strata to recruit White and Black American men and women ≥45 years old representing the USA 'stroke belt' (North Carolina, South Carolina, Georgia, Arkansas, Tennessee, Alabama, Mississippi and Louisiana) and non-stroke belt regions of the contiguous 48 USA states. REGARDS was conducted according to the guidelines laid down in the declaration of Helsinki, and all procedures involving human subjects/patients were approved by the university of Alabama-Birmingham institutional review board (approval # IRB-020925004). Written informed consent was obtained from all study participants at enrollment. The telephone response and cooperation rates[17] were 33 % and 49 %, respectively[18]. A total of 30 239 participants were initially enrolled. After enrollment, information on participant demographics, medical history and lifestyle behaviours (physical activity, alcohol consumption, social network size, sedentary behaviour and smoking history) were collected via computer-assisted telephone interviews, followed approximately 3–4 weeks later by an in-home visit conducted by trained study staff to conduct anthropometry, including waist circumference, and measure blood pressures. During the in-home visit, participants were also given the previously validated, self-administered 110-item Block98 FFQ to assess their usual diet over the past year, to complete and return by mail[19]. Total energy and nutrient intakes were calculated by adding energy and nutrients from all food and supplement sources using the dietary database developed by Block *et al.*[20] and maintained by NutritionQuest[21]. Physical activity and alcohol intakes were assessed via open-ended questions regarding how many times per week the participant engaged in physical activity intense enough to work up a sweat (a previously validated measure)[22,23] and on current consumption of alcoholic beverages (reported as drinks per day, week, month or year), respectively. Self-reported measures of alcohol intake were previously shown to be reasonably valid[24,25]. Sedentary behaviour was assessed via the self-reported average number of hours the participant spent watching television or video[26] (response choices were none, > 0–6 h/week, 1 h/d, 2 h/d, 3 h/d and 4+ h/d). Social network size was assessed via two open-ended questions regarding the self-reported number of friends and relatives the participant felt 'close' to (i.e. 'feel at ease with, can talk to about private matters, and can call on for help')[27]

Of the 30 239 participants enrolled, for the present analyses, we excluded those with data anomalies (*n* 56), missing dietary data (*n* 8547) or lifestyle EC components (*n* 1810), with an implausible waist circumstance (≤ 51 cm) (*n* 20), with a BMI < 18·5 kg/m^2 (*n* 207), lost to follow-up (*n* 168) or diagnosed with CHD (*n* 3287) or stroke (*n* 677) at baseline, yielding an analytic sample of 15 467 participants (51·2 % of cohort participants). The characteristics of the excluded participants were similar to those included except that they were more likely to have comorbid conditions, be Black American and have incomes < $20k (the latter two were mostly attributable to missing FFQ data).

Evolutionary-concordance score components and calculations

Details of the construction of the equal-weight, multicomponent total EC score were previously published[13] and are summarised below. A seven-component total EC score, which included one thirteen-component dietary EC score and six major lifestyle factors (alcohol intake, physical activity, sedentary behaviour, excess adiposity, smoking history and social network size), was developed to reflect overall closeness to a more evolutionary-concordant total (including lifestyle and diet) pattern[13]. A lifestyle EC score limited to the six non-dietary major lifestyle factors was also calculated. Details on how each of the EC score's components was calculated and scored are described below and summarised in Table 1. Briefly, we first categorised each of the seven components into five categories, as described further below, which we assigned values from 1 to 5, with higher scores indicating greater evolutionary concordance, and then we summed the individual components' scores such that the total score could range from 7 to 35.

As previously described, the thirteen-component dietary EC score, with a possible range from 13 to 65, was calculated using FFQ data[11], except that alcohol was excluded from the diet score[13]. Briefly, each of the thirteen dietary components (online Supplemental Table 1) was divided into quintiles based on the sex-specific distribution of intakes at baseline. For the lowest to the highest quintile, respective scores of 1–5 were assigned for dietary exposures for which higher intakes were considered more evolutionarily concordant (vegetables, fruits, lean meats, fish, nuts, diversity of fruits and vegetables and Ca (calculated as the residuals from the regression of total Ca intake on total dairy intake to account for Ca intake fully adjusted for dairy intake)), and scores of 5–1 for dietary exposures for which lower intakes were considered more evolutionarily concordant (red/processed meats, dairy products, grains, baked goods, sugar-sweetened beverages and Na). These values were then summed,

Table 1. Components and construction of the total evolutionary-concordance score* in the REasons for Geographic and Racial Differences in Stroke cohort study (REGARDS)

		Total evolutionary-concordance score points				
Component category	Component	1	2	3	4	5
Lowest value "best"	Alcohol intake, drinks/wk.					
	Men	≥7·5	3·0–7·0	1·0–3·0	> 0·0–< 1·0	0
	Women	≥6·0	2·0–5·0	0·5–1·75	> 0·0–< 0·5	0
	Sedentary behaviour†, hrs./d	≥4	3	2	1	< 1
	Smoking history, pack-yrs.	≥35·0	16·0–34·9	4·5–15·9	< 4·5	0
	Waist circumference‡ cm					
	Men	≥109·0	101·6–108·9	95·9–101·5	89·0–95·8	60·9–88·9
	Women	≥104·2	94·1–104·1	86·1–94·0	78·6–86·0	55·9–78·5
Highest value "best"	Dietary EC score§	17–33	34–37	38–40	41–44	45–60
	Physical activity‖, times/wk.	0	1–2	3–4	5–6	≥7
	Social network size¶	0–5	6–7	8–11	12–17	≥18

hrs., hours; yrs., years; EC, evolutionary-concordance; wk., week.
* The possible range for the seven-component score was 7–35; a higher score indicates a more evolutionary-concordant lifestyle pattern.
† Self-reported average hours per week spent watching television or video (none, 1–6 h/week, 1 h/d, 2 h/d, 3 h/d and ≥ 4 h/d); response categories 'none' and '1–6 h/week' combined for inclusion in a five-point scale.
‡ Measured by trained personnel during an in-home visit.
§ See text and online Supplemental Table 1 for details on the construction of the thirteen-component diet score; of a possible score range of 13 to 65, the actual score range in the study population was 17–60; a higher score indicates a more evolutionary-concordant dietary pattern.
‖ Self-reported times per week the participant engaged in physical activity intense enough to work up a sweat (open-ended).
¶ Self-reported number of friends and relatives the participant felt 'close' to (open-ended).

with a higher score indicating a more evolutionary-concordant diet pattern. When included as a total EC score component, the dietary EC score was categorised according to quintiles of its distribution in the analytic population at baseline, and the quintiles assigned values of 1–5, with a higher score indicating higher evolutionary concordance.

To calculate the total EC score, we first categorised the information on the six non-dietary lifestyle factors as described below, and then assigned scores to each category according to the values shown in Table 1. From self-reported information on current alcohol intake (drinks per week), we categorised alcohol intake as none and sex-specific quartiles among those who drank. We defined never smokers as those who reported smoking < 100 cigarettes in their lifetime and categorised former and current smokers according to quartiles of smoking pack-years (calculated by multiplying the average number of packs smoked per day by the years smoked). To reflect excess adiposity for our analyses, we used waist circumference rather than BMI (waist circumference was more directly associated with risk for various outcomes in REGARDS than was BMI[13,28], and hip circumference was not measured). We categorised waist circumference (cm), measured by trained personnel during the in-home visit, according to sex-specific quintiles. Given the limited response options for physical activity and sedentary behaviour, we combined responses according to intervals shown in Table 1. We then summed the values for the six lifestyle components and the dietary EC component to yield the total EC score, with a higher score indicating higher overall evolutionary concordance.

Collection of outcome information and time to follow-up

Our primary outcome of interest was incident CVD, defined as the first occurrence of CHD (fatal or non-fatal myocardial infarction or death due to CHD), or stroke (fatal or non-fatal, ischaemic or haemorrhagic). We also considered incident CHD and stroke separately as secondary outcomes of interest in the present study. Briefly, study participants or their designated proxies were contacted by study staff every 6 months to ascertain CVD events and deaths[16]. For reported hospitalisations, physician visits and deaths, REGARDS personnel retrieved medical records, death certificates and autopsy reports, and CVD events and related deaths were adjudicated by a committee of trained adjudicators[16].

We calculated follow-up time as the time between the date of baseline questionnaire completion and the date of a CHD or stroke diagnosis (for CVD analyses, for participants who became diagnosed with both, we used the date of the first diagnosis), the date of death or the end of the last follow-up (31 December 2017), whichever was first.

Statistical analyses

Main analyses. We summarised participant characteristics at baseline overall and by total EC score quintiles, using descriptive statistics. To investigate associations of the total, dietary and lifestyle EC score quintiles with incident CVD, CHD and stroke, we used multivariable Cox proportional hazards regression models to calculate adjusted hazards ratios (HR) and their corresponding 95 % CI. We included the median values of each score quintile as continuous variables in corresponding models to test for trend. We also estimated the cumulative incidence of CVD, CHD and stroke, using methods for competing risks analysis in all models[29,30] and reported it within quintiles of the total, dietary and lifestyle EC scores.

We identified potential model covariates based on biological plausibility and previous literature. In all multivariable models, we adjusted for age (years), race (Black, White), annual household income (< $20k, 20–34k, 35–74k, ≥75k, missing), education status (< high school, high school, some ≥college and ≥college), health insurance (yes/no), sex/current postmenopausal hormone (PMH) use (male, female with PMH use, female

without PMH use), region of residence (stroke belt/non-stroke belt), statin use (yes/no), family history of CVD in a first-degree relative (yes/no), regular (≥twice/week) aspirin use (yes/no), regular (≥twice/week) non-aspirin non-steroidal anti-inflammatory drug (NSAID) use (yes/no), total energy intake (kcal/d), history of diabetes mellitus (yes/no), history of hypertension (yes/no), baseline systolic and diastolic blood pressures (mmHg), history of cancer (yes/no) and history of kidney failure (yes/no). Approximately 11 % of participants were missing data on income, so we conducted analyses using a missing indicator variable for missing income (< 5 % were missing data on all other covariates, so missing indicators were not used for those variables). The dietary EC score model additionally adjusted for the individual lifestyle EC score components (alcohol intake, smoking history, waist circumference, physical activity, sedentary behaviour and social network). The lifestyle EC score model additionally adjusted for the dietary EC score. We assessed proportional hazards assumptions using Schoenfeld residuals for each exposure and covariate.

Supplemental and sensitivity analyses. We conducted stratified analyses to assess whether the associations of total EC score quintiles with incident CVD, CHD and stroke differed by categories of selected participant characteristics at baseline. For these analyses, we stratified on sex, age (< 65/≥ 65 years), race (Black/White), region (stroke belt/non-stroke belt), comorbidity conditions (defined as cancer, kidney failure, diabetes, statin user or hypertension) (yes/no) and smoking status (ever/never smoked). We included EC score quantile x stratification factor interaction terms in the Cox proportional hazards regression models to assess potential multiplicative statistical interaction; to test for the statistical significance of the interaction terms, we used likelihood ratios based on models with and without the interaction terms. For the analysis stratified on smoking status, we excluded smoking from the total EC score and additionally adjusted for smoking history (pack-years) for those who ever smoked. For the analysis stratified on comorbidity status, since the number of cases in the 'no comorbidity' stratum was small, we analysed that stratum according to total EC score tertiles; to facilitate comparisons across comorbidity strata and between the 'yes comorbidity' stratum and strata of other stratification factors, we categorised the 'yes comorbidity' stratum according to total EC score tertiles and quintiles.

We also conducted several sensitivity analyses. To investigate the relative importance of each of the total EC score's components, we first assessed the multivariable-adjusted associations of the seven independent components in the EC score – each modeled using the five categories described in Table 1 – with incident CVD. The model for each individual score component additionally adjusted for the other six components. Second, we removed individual components from the total EC score (with replacement) one at a time and estimated the associations of the seven reduced scores (each comprising six components) with incident CVD. We then calculated the proportional change in the estimated association of the highest relative to the lowest quintile of each reduced EC score with incident CVD from that for the original total EC score as follows: $(HR' - HR)/HR \times 100\,\%$, where *HR'* is the HR for a reduced EC score–CVD association, and *HR* is the HR for the original total EC score–CVD association. As a final sensitivity analysis, to rule out potential reverse causation bias, we excluded participants who became newly diagnosed with CVD within the first year of follow-up.

We conducted all analyses using SAS, version 9.4 (SAS Institute). All *P*-values were two-sided. We considered *P*-values ≤ 0·05 or 95 % CI that excluded 1·0 statistically significant.

Results

During follow-up (median 11·0 years, range 0·1–14·8 years), a total of 1563 participants were diagnosed with CVD (967 with CHD, 596 with stroke). Participants in the higher relative to the lower total EC score quintiles were more likely to be White, female, less formally educated, without comorbid conditions, have incomes < $20k/year and take PMH (among women) and, on average, had a lower BMI (Table 2).

Associations of the evolutionary-concordance scores with incident CVD, CHD and stroke

Age- and multivariable-adjusted associations of the total, dietary and lifestyle EC scores with incident CVD, CHD and stroke are presented in Table 3. There were statistically significant trends for decreasing hazards of incident CVD, CHD and stroke with an increasing total EC score, and the point estimates for all three outcomes were nearly identical. For example, among participants in the highest relative to the lowest total EC score quintile, the multivariable-adjusted hazards of incident CVD, CHD and stroke over the follow-up period were statistically significantly 27 %, 28 % and 24 % lower, respectively. There also were statistically significant trends for decreasing hazards of incident CVD with increasing dietary and lifestyle EC scores, although the estimated associations were more modest than those for the total EC score. For example, among participants in the highest relative to the lowest dietary and lifestyle EC score quintiles, the multivariable-adjusted hazards for CVD were statistically significantly 16 % and 21 % lower, respectively. The estimated inverse associations of the dietary and lifestyle EC scores with CHD and stroke were also more modest than those for the total EC score, but only the findings for the lifestyle EC score were statistically significant.

Throughout the study follow-up period, individuals with higher total, dietary and lifestyle EC scores had a lower cumulative incidence of CVD, CHD and stroke than those with lower scores (online Supplemental Fig. 1), consistent with the estimated HR in Table 2. The 14-year cumulative incidences for CVD, CHD and stroke among those in the highest relative to the lowest total EC score quintile were 15·3 % *v.* 11·5 %, 11·0 % *v.* 7·8 % and 5·7 % *v.* 4·8 %, respectively (online Supplemental Fig. 1 and Supplemental Table 2).

Stratified and supplemental analyses

There were no statistically significant or substantial differences in the total EC score–incident CVD associations according to subgroups of selected participant characteristics (online Supplemental Table 3). However, there were some suggestions that the inverse total EC score–incident CVD associations were

Table 2. Selected characteristics of the participants according to quintiles of the total evolutionary-concordance (EC) score at baseline (2003–2007) in the REGARDS cohort study (Percentages; mean values and standard deviations, *n* 15 467)

				Total evolutionary-concordance score quintiles†													
	Total			1			2			3			4			5		
	(*n* 15 467)			(*n* 3549)			(*n* 2469)			(*n* 2748)			(*n* 3749)			(*n* 2952)		
Characteristics*	%	Mean	SD	%	Mean	SD	%	Mean	SD	%	Mean	SD	%	Mean	SD	%	Mean	SD
Age, years		63·8	9·1		63·1	8·8		63·7	9·1		64·0	8·9		64·0	9·3		64·2	9·1
Male, %	40·6			44·6			40·6			41·0			38·2			38·6		
White race, %	66·3			61·8			62·2			63·8			68·7			74·5		
≥High school graduate, %	60·2			71·4			65·0			61·4			54·9			48·4		
Income < $20K, %	14·2			20·3			16·4			14·0			11·9			8·2		
Stroke belt region‡, %	56·2			55·6			55·3			56·7			56·5			57·2		
Has health insurance, %	93·5			91·1			92·8			93·3			94·7			95·5		
Take PMH (women only)§, %	59·6			55·7			55·5			62·4			60·6			63·3		
Regularly‖ take aspirin, %	38·2			38·1			37·1			40·1			38·4			37·0		
Regularly‖ take NSAID, %	15·7			19·0			17·0			15·4			13·8			13·2		
Currently smoke, %	12·7			27			16·0			10·2			6·7			2·9		
Total energy intake, kcal/d		1714	709		1854	752		1759	740		1722	714		1643	669		1590	636
Dietary EC score¶		39·0	6·1		35·4	5·3		37·4	5·6		38·9	5·6		40·6	5·6		43·1	5·4
Alcohol intake, drinks/week		2·4	6·8		4·4	10·1		2·5	6·3		2·3	6·2		1·6	4·9		0·9	2·9
Waist circumference, cm		94·9	15·1		103·1	14·9		98·7	14·9		95·4	13·9		91·5	13·5		85·7	11·9
BMI, kg/m^2		29·2	6·0		31·6	6·6		30·4	6·3		29·3	5·8		28·2	5·3		26·2	4·4
Physical activity**, times/week		2·5	2·3		1·2	1·8		1·9	2·1		2·5	2·3		3·0	2·3		4·0	2·2
TV/screen time > 2 h/week, %	55·8			83·0			68·6			60·7			44·7			21·8		
# Close friends or family		13·1	15·0		8·2	8·4		11·1	11·3		12·7	12·3		14·8	13·1		19·0	23·7

EC, evolutionary-concordance; REGARDS, REasons for Geographic and Racial Differences in Stroke; PMH, postmenopausal hormone; NSAID, non-steroidal anti-inflammatory drug; TV, television.
* Values presented are mean (SD) or percentages. The following variables had missing values: income (11.0 %), insurance (0.1 %), regular NSAID use (0.3 %), regular aspirin use (0.1 %).
† See text and Table 1 for details; total EC score quintile ranges were quintile 1, 7–18; quintile 2, 19–20; quintile 3, 21–22; quintile 4, 23–25; quintile 5, 26–35; a higher score indicates a more evolutionary-concordant lifestyle pattern.
‡ North Carolina, South Carolina, Arkansas, Georgia, Tennessee, Alabama, Mississippi and Louisiana.
§ PMH use is described among women only (*n* 9184). The denominators used to calculate the percentage of women who used PMH within total EC score quintiles were quintile 1, *n* 1966; quintile 2, *n* 1466; quintile 3, *n* 1621; quintile 4, *n* 2317; quintile 5, *n* 1814.
‖ At least twice/week.
¶ See online Supplemental Table 1 for details; of a possible score range of 13 to 65, the actual score range in the study population was 17–60; a higher score indicates a more evolutionary-concordant dietary pattern.
** Self-reported times per week the participant engaged in physical activity intense enough to work up a sweat.

Table 3. Associations of evolutionary-concordance (EC) scores with incident CVD, CHD and stroke among participants in the REGARDS cohort study (*n* 15 476), 2003–2017 (Hazards ratios and 95 % confidence intervals)

	CVD†					CHD					Stroke				
EC scores* and quintiles (quintile ranges)	# Cases	Age-adjusted HR	95 % CI‡	Multivariable-adjusted HR	95 % CI§	# Cases	Age-adjusted HR	95 % CI‡	Multivariable-adjusted HR	95 % CI§	# Cases	Age-adjusted HR	95 % CI‡	Multivariable-adjusted HR	95 % CI§
Total EC score															
1 (7–18)	417	1·00 (ref.)		1·00 (ref.)		277	1·00 (ref.)		1·00 (ref.)		165	1·00 (ref.)		1·00 (ref.)	
2 (19–20)	278	0·90	0·77, 1·04	0·97	0·83, 1·13	162	0·79	0·65, 0·96	0·86	0·71, 1·05	131	1·06	0·84, 1·33	1·12	0·89, 1·41
3 (21–22)	295	0·83	0·71, 1·96	0·92	0·79, 1·07	177	0·75	0·62, 0·91	0·84	0·70, 1·02	136	0·96	0·77, 1·21	1·03	0·82, 1·30
4 (23–25)	330	0·65	0·56, 0·75	0·75	0·65, 0·87	194	0·58	0·48, 0·69	0·68	0·57, 0·82	155	0·76	0·61, 0·95	0·85	0·68, 1·07
5 (26–35)	243	0·59	0·50, 0·75	0·73	0·62, 0·86	157	0·57	0·47, 0·70	0·72	0·59, 0·89	103	0·62	0·49, 0·80	0·76	0·59, 0·98
P_{trend}‖		< 0·001		< 0·001			< 0·001		< 0·001			< 0·001		0·02	
Dietary EC score															
1 (17–33)	306	1·00 (ref.)		1·00 (ref.)		199	1·00 (ref.)		1·00 (ref.)		119	1·00 (ref.)		1·00 (ref.)	
2 (34–37)	357	0·92	0·79, 1·07	0·97	0·83, 1·14	210	0·84	0·69, 1·01	0·89	0·73, 1·08	171	1·12	0·89, 1·42	1·14	0·90, 1·44
3 (38–40)	322	0·93	0·80, 1·09	1·02	0·87, 1·20	207	0·93	0·76, 1·13	1·02	0·84, 1·25	133	0·98	0·76, 1·26	1·05	0·81, 1·35
4 (41–44)	332	0·78	0·67, 0·91	0·90	0·76, 1·06	196	0·71	0·59, 0·87	0·84	0·68, 1·03	161	0·96	0·76, 1·21	1·05	0·82, 1·35
5 (45–60)	246	0·66	0·56, 0·78	0·84	0·70, 0·99	155	0·64	0·52, 0·79	0·85	0·69, 1·08	106	0·72	0·56, 0·94	0·85	0·64, 1·13
P_{trend}‖		< 0·001		0·03			< 0·001		0·16			0·004		0·21	
Lifestyle EC score															
1 (6–15)	372	1·00 (ref.)		1·00 (ref.)		237	1·00 (ref.)		1·00 (ref.)		156	1·00 (ref.)		1·00 (ref.)	
2 (16–17)	310	0·94	0·81, 1·09	0·99	0·85, 1·16	194	0·92	0·76, 1·12	0·99	0·81, 1·20	135	0·97	0·77, 1·22	1·01	0·80, 1·27
3 (18–19)	289	0·71	0·61, 0·83	0·79	0·68, 0·93	176	0·68	0·56, 0·83	0·78	0·64, 0·95	133	0·77	0·61, 0·97	0·84	0·67, 1·06
4 (20–21)	272	0·71	0·60, 0·82	0·83	0·70, 0·97	154	0·63	0·51, 0·77	0·75	0·61, 0·92	127	0·78	0·61, 0·98	0·88	0·69, 1·11
5 (22–30)	320	0·64	0·55, 0·74	0·79	0·67, 0·92	206	0·54	0·54, 0·78	0·81	0·67, 0·98	139	0·66	0·52, 0·83	0·79	0·62, 1·00
P_{trend}‖		< 0·001		< 0·001			< 0·001		0·004			< 0·001		0·04	

EC, evolutionary-concordance; REGARDS, REasons for Geographic and Racial Differences in Stroke; HR, hazards ratio; ref., reference.

* For construction of scores, see text and Table 1; a higher score indicates a more evolutionary-concordant lifestyle pattern; lifestyle EC score comprised all score components in Table 1 except for the dietary EC score.

† CVD includes CHD and stroke.

‡ From Cox proportional hazards model, adjusted only for age (years).

§ From multivariable Cox proportional hazards models. All fully adjusted models adjusted for age (years), race (Black/White), income (< $20 k, 20–34 k, 35–74 k, ≥75 k, missing), education status (< high school, high school, some college, ≥college), health insurance (yes/no), sex/postmenopausal hormone use (male, female with postmenopausal hormone use, female without postmenopausal hormone use), statin use (yes/no), baseline systolic and diastolic blood pressures (mmHg), region (stroke belt/non-stroke belt), history of diabetes mellitus (yes/no), history of hypertension (yes/no), history of cancer (yes/no), history of kidney failure (yes/no), regular (twice/week or more) aspirin use (yes/no), regular (twice/week or more) non-aspirin NSAID use (yes/no), total energy intake; the model for CHD was additionally adjusted for family history of CHD in a first-degree relative (yes/no), the model for stroke was additionally adjusted for family history of stroke in a first-degree relative (yes/no), and the model for CVD was additionally adjusted for family history of CVD (CHD or stroke) in a first-degree relative (yes/no). The dietary EC score model was additionally adjusted for the six individual lifestyle EC score components (alcohol, smoking, waist circumference, physical activity, sedentary behaviour and social network size; see Table 1 for details). The lifestyle EC score model was additionally adjusted for the dietary EC score.

‖ P_{trend} calculated by including the median values of the EC score quintiles as a continuous variable in the corresponding model.

slightly stronger among Black participants, those residing in the USA stroke belt region, and those with a comorbidity at baseline, but the 95 % CI for the corresponding HR across these strata overlapped considerably (online Supplemental Table 3).

Associations of 1) the total EC score's individual components and 2) the reduced EC scores, after removing (and replacing) each of the seven components from the total EC score one at a time, with incident CVD are summarised in Supplemental Table 4. Of the individual score components, smoking, followed by waist circumference and then diet, was most strongly associated with incident CVD; among those in the highest relative to the lowest category of smoking and waist circumference, the HR (95 % CI) were 1·52 (1·32, 1·76), 1·27 (1·07, 1·50) and 0·84 (0·70, 1·00), respectively. No single component appeared to account for our findings; however, removal of smoking, waist circumference and diet from the total EC score attenuated the inverse EC score–CVD risk association most (by 15·1 %, 9·6 % and 6·8 %, respectively). However, removal of sedentary behaviour and social network size (which individually were not associated with CVD risk) from the total EC score strengthened the inverse EC score–CVD risk association. In post hoc analyses, concurrent removal of sedentary behaviour and social network size from the total and lifestyle scores further strengthened the associations of those EC scores with CVD risk; for example, among those in the highest relative to the lowest reduced total and lifestyle EC score quintiles, the HR (95 % CI) were 0·67 (0·57, 0·80) and 0·67 (0·56, 0·79), respectively. Excluding participants who became newly diagnosed with CVD during the first year of follow up had only minimal effects on our results (online Supplemental Table 5).

Discussion

Our findings support that a more evolutionary-concordant diet and lifestyle pattern may be associated with lower CVD, CHD and stroke risk among Black and White men and women. Also, in our study, among the seven individual components of our EC score, tobacco smoking contributed the most to the total EC score–incident CVD association, followed by waist circumference (as a marker of central adiposity) and then diet.

Previous evidence from basic science and epidemiologic literature supports that each component of our total EC score could be plausibly linked to lower risk of CVD, including CHD and stroke. An evolutionary-concordant dietary pattern is characterised by higher intakes of fruits and vegetables, nuts and fish – all foods that may be linked to lower CVD risk[31,32] via their antioxidative and anti-inflammatory properties[33–36]. An evolutionary-concordant dietary pattern is also characterised by lower consumption of high fat meats, which are associated with higher CVD risk[37,38]. Modern red and processed meats are high in saturated fats, which are associated with higher oxidative stress and inflammation[39–41]. Substantial literature supports that physical activity is inversely associated with CVD risk[42,43]; this association may be due to physical activity's contribution to energy balance (and thus adiposity), lower risk lipid/lipoprotein profiles and lower systemic inflammation[44,45]. Tobacco smoking and heavy alcohol consumption may increase oxidative stress[46–48]. Excess central adiposity (assessed as waist circumference in the present study) is associated with higher CVD risk[49,50], possibly via higher inflammation and adverse effects on hormones levels and metabolism[51]. Previous meta-analyses suggested that longer sedentary time is associated with higher CVD risk[52,53], possibly via several potential mechanisms, including glucose metabolism and inflammatory and oxidative stress pathways[54]. Social isolation may be linked to CVD development via several mechanisms, such as causing changes to vascular stress responses and reduced inflammatory responses[55,56]. A recent meta-analysis supports that social isolation may be associated with higher CVD risk[57].

In our study, consistent with the *evolutionary discordance hypothesis,* participants with lifestyles considered to be the most evolutionary-concordant had approximately 30 % lower CVD risk than those with lifestyles considered to be the least concordant. Previous studies or reviews have reported dietary[58–60] or lifestyle[61–66] patterns/scores that were similar to our EC scores, and their results support our findings of an inverse association of overall more evolutionary-concordant ('healthier') lifestyle patterns with CVD risk[58–66]. Despite the differences in the construction of these scores, most of these previously reported lifestyle scores/patterns were developed based on consensus healthy standards and have some common components (e.g. diet, tobacco smoking and physical activity)[58–66].

To our knowledge, only two reported studies investigated an association of an EC diet pattern ('Paleolithic diet' pattern) with CVD[14,15]. Consistent with our results, a prospective cohort study among Spanish adults (n 18 210) reported a statistically significant association of an EC dietary score with incident CVD ($HR_{Q5\ vs.\ Q1} = 0{\cdot}45$ 95 % CI, 0·27, 0·76; $P_{trend} = 0{\cdot}007$)[15]. Inconsistent with our results, a cross-sectional study among Australian adults (n 5376) reported a null association of an evolutionary-concordant diet pattern with prevalent CVD (OR = 1·08; 95 % CI, 0·71–1·65; $P_{trend} = 0{\cdot}65$)[14]. The inconsistency could be due to the different study design (cross-sectional rather than prospective) and outcome (prevalence rather than incidence) or to study population differences. Neither of the two studies investigated non-dietary factors as score components[14,15]. Three previous studies investigated and reported associations of evolutionary-concordant lifestyle patterns with other chronic diseases (colorectal cancer)[10] or mortality[12,13]. A more evolutionary-concordant lifestyle pattern score (comprising physical activity, BMI and tobacco use), alone and jointly with a more evolutionary-concordant diet pattern score (comprising 14 components), was associated with lower risk of incident colorectal cancer[10] and all-cause, all-CVD and all-cancer mortality[12] in the prospective Iowa Women's Health Study (n 35 221 White women, ages 55–69 years). The prospective REGARDS cohort study also reported statistically significant inverse associations of the identical EC score used in the present study with all-cause, all-CVD and all-cancer mortality[13].

In the present study, we found that for each given EC score, its estimated inverse associations with CHD and stroke (and thus CVD) incidence were of similar magnitude, suggesting the possibility of approximately equal importance of diet and lifestyle to both CHD and stroke (and thus CVD) incidence, and thus to their

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prevention. We also estimated that the total EC score was most strongly associated with the three outcomes, followed by the lifestyle score, then the diet score. While these findings suggest that lifestyle may contribute more strongly than diet to CVD risk, they also support that both contribute to CVD risk and thus that adopting a combination of more evolutionary-concordant diets and lifestyle behaviours may help minimise it.

No single total EC score component appeared to account for our findings, and most components, though not all (e.g., sedentary behaviour and social network size), were estimated to be associated with CVD risk. However, among the seven EC score components, smoking, followed by waist circumstance and then diet individually were most strongly associated with incident CVD and their removal from the total EC score most strongly attenuated the total EC score–CVD association. Inclusion of sedentary behaviour and social network size in the total EC score attenuated the association of the score with CVD. The findings for all but sedentary behaviour and social network size are consistent with previous literature[59–66]. Evidence from basic science literature suggests that sedentary behaviour and social isolation are biologically linked to CVD risk[55,56], and recent epidemiologic studies and meta-analyses support that longer sedentary times[53,54] and higher social isolation[55–57] are associated with higher CVD risk. In our study, we did not have a comprehensive assessment of sedentary behaviour, so we used time spent watching television as a surrogate. This may have resulted in exposure misclassification, which would have attenuated our results for sedentary behaviour, and by extension the lifestyle score. Similarly, not having a comprehensive assessment of social connectiveness, we used social network size as a surrogate, which may also have attenuated our results. We also note that physical activity was estimated to be only modestly, not statistically significantly, inversely associated with CVD risk, but did contribute to the strength of the inverse total EC score–incident CVD association. We further note that physical activity was assessed via a single open-ended question regarding how many times per week the participant engaged in physical activity intense enough to work up a sweat. Although this measure of physical activity was previously validated[22,23] and found to be statistically significantly inversely associated with all-cause mortality in REGARDS[13], it may have been a less accurate measure than was used in other study populations; such measurement error could have led to an under-estimate of the contribution of physical activity to CVD risk. We note that the emphasis of our analyses and paper is on the collective contributions of multiple exposures for which evolutionary discordance is known, and as hypothesised, found that the total EC score was strongly inversely associated with CVD, CHD and stroke risk. We hypothesise that measuring all total EC score components with the highest levels of validity and in populations with a wide diversity of exposures (given that the scores are calculated based on within-study population differences) would yield stronger inverse total EC score–CVD risk associations than was found in the present study, thus supporting the role of evolutionary discordance in the aetiology of CVD.

Strengths of our study include the prospective design and large, diverse, well-characterised study population. Also, for reported hospitalisations, physician visits and deaths, REGARDS personnel retrieved medical records, death certificates and autopsy reports, and CVD events and related deaths were adjudicated by a committee of trained adjudicators according to a strict protocol[16], thus reducing outcome misclassification. To our knowledge, this is the first investigation of an EC score that includes dietary and lifestyle factors with incident CVD, CHD and stroke. In addition to the limitations of our sedentary behaviour, social network size and physical activity variables discussed above, our study has other limitations. First, the diet and all lifestyle score components, except waist circumference, were self-reported, and all exposure information was collected only at baseline, which may have produced misclassification error. However, this would be regarded as non-differential in a prospective study, and generally attenuates estimated associations. Second, as with most diet or lifestyle 'pattern' scores, we assigned equal weights to the EC score components, but each score component may not contribute equally to the outcomes. Third, our results may not be generalisable to the entire USA population, as all participants agreed to participate in a long-term study, and Black participants and those living in the USA 'stroke belt' region were oversampled. However, we observed no statistically significant differences in the total EC score–CVD association by race or residential region. Finally, we had no information on occupational exposures, and as with all observational studies, residual confounding cannot be ruled out.

In conclusion, our findings, combined with those from previous studies, suggest that a more evolutionary-concordant diet and lifestyle pattern may be associated with lower CVD, CHD and stroke risk among White and Black men and women. Of our seven EC score components, not smoking, not having excess central adiposity and having a more evolutionary-concordant diet (e.g. higher intakes of various fruits and vegetables, fish, lean meat and nuts and lower intakes of red and processed meat, dairy products and sugar-sweetened beverages) most strongly contributed to our findings of an inverse total EC score–CVD risk association. For future investigations of associations of EC scores with CVD risk, more comprehensive, precise assessments of sedentary behaviours, social connectiveness, and perhaps physical activity and adiposity, are needed.

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All authors contributed to the study conception and design, data interpretation, and manuscript writing. R. M. B. and Z. M. were primarily responsible for the project conception and design. S. J., J. M. S., E. B. L. and M. M. S. collected the data. Z. M. and A. N. T. were primarily responsible for data analyses. Z. M. and R. M. B. were primarily responsible for interpreting the data and writing the manuscript. R. M. B. supervised the analysis project and manuscript writing. All authors read and approved the final manuscript.

Supplementary material

For supplementary material/s referred to in this article, please visit https://doi.org/10.1017/S0007114522002549

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