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# Association between diet quality and incident cardiovascular disease stratified by body mass index



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# ABSTRACT

*Objective:* Diet quality is a significant contributor to cardiovascular disease (CVD) development given its substantial influence on important downstream CVD mediators such as weight. However, it is unclear if there are additional pathways between diet quality and incident CVD independent of weight. We sought to determine if higher diet quality was associated with lower CVD risk stratified by BMI categories. *Methods:* Prospective cohort data from the Lifetime Risk Pooling Project (LRPP) was analyzed. Diet data from 6 US cohorts were harmonized. The alternative Healthy Eating Index-2010 (aHEI-2010) score was calculated for each participant. Within each cohort, participants were divided into aHEI-2010 quintiles. The primary outcome of interest was composite incident CVD event including coronary heart disease, stroke, heart failure, and CVD death. Cox regression analysis was performed separately for three BMI strata: 18.5−24.9, 25−29.9, and ≥ 30 kg/m<sup>2</sup>.

*Results*: A total of 30,219 participants were included. During a median follow-up of 16.2 years, there were a total of 7,021 CVD events. An inverse association between aHEI-2010 score and incident CVD was identified among participants who were normal weight (comparing highest quintile with lowest quintile: adjusted hazard ratio [95% confidence interval] 0.57 [0.50 - 0.66]) and among participants with overweight (0.69 [0.61 - 0.77]). aHEI-2010 score was not associated with CVD among participants with obesity (0.97 [0.84 - 1.13]).

*Conclusions:* Among adults in the United States, higher diet quality as measured by aHEI-2010 was significantly associated with lower risk of incident CVD among individuals with normal weight and overweight but not obesity.

# 1. Introduction

Diet, a modifiable risk factor, is an important target for reducing the incidence of cardiovascular disease (CVD) and increasing healthy years free of chronic disease[1]. High-quality randomized control trials (RCT) and meta-analyses have shown that diets high in fruits, vegetables, and fiber and low in sodium are associated with lower weight, itself a major risk factor for CVD[2–7]. However, low-sodium diets high in fruits, vegetables, and fiber have also been hypothesized to mediate benefits for cardiovascular disease prevention separate and independent of its effect on weight. For example, diets high in polyphenols, polyunsaturated fats and antioxidants have been associated with lower levels of inflammation, improved lipid profiles, lower blood pressure, and reduced blood glucose levels regardless of weight status[8].<sup>(9)</sup> Despite this, the inde-

pendent association of diet and CVD, within BMI subgroups, has been less studied, particularly in a large, diverse sample size. In the present study, we used large, pooled cohort data to describe the independent association between diet quality and incident CVD in a racially and ethnically diverse population. We hypothesized that a higher quality diet is associated with a lower incidence of CVD independent of BMI.

## 2. Methods

This study was fully reviewed and approved by the institutional review board at Northwestern University for the use of this de-identified dataset. Written informed consent was obtained from all participants for initial data collection in each individual cohort.

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Abbreviations: CVD, cardiovascular disease; LRRPP, Lifetime Risk Pooling Project; aHEI-2010, alternative Healthy Eating Index-2010; RCT, randomized control trials; BMI, body mass index.

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## 2.1. Study Sample

This study included data from the Cardiovascular Lifetime Risk Pooling Project (LRPP). Detailed methods for the LRPP are described elsewhere[10]. Briefly, the LRPP included 20 community-based prospective cohorts of US participants from 1948 to 2004 in an effort to study longterms risks of CVD[10]. Six cohorts that assessed usual dietary intake and had information on study variables were included for this analysis. The cohorts included were the Atherosclerosis Risk in Communities (ARIC) Study[11], Coronary Artery Risk Development in Young Adults (CARDIA) Study[12], Cardiovascular Health Study (CHS)[13], Framingham Heart Study (FHS)[14], Framingham Offspring Study (FOS)[15], and Multi-Ethnic Study of Atherosclerosis (MESA)[16] (Supplemental Table 1). Participants were excluded if they were underweight (BMI < 18.5), had CVD at baseline, missing data, or baseline dietary intake was not performed.

## 2.2. Diet Data Assessment

Diet data were harmonized cohort by cohort using a standardized protocol and data dictionary as detailed previously[17]. Briefly, consumption frequencies were converted into estimated daily servings using an average value. For example, a food group that was consumed 3-4 times per week was converted to 0.5 times per day. In one of the cohorts, descriptive portion sizes were used and thus "small", "medium", and "large" serving sizes were assigned a weight of 0.5, 1.0, and 1.5, respectively. Food groupings were constructed using standard definitions. Ingredients from mixed dishes were considered. After diet harmonization, participants were scored based on the alternative Healthy Eating Index 2010 (aHEI-2010) scoring algorithm which ranges from 0 [lowest quality diet scores] to 110 [highest quality diet score] (Supplemental Table 2)[18]. Baseline measurements were defined as the first available diet data collection visit for each cohort and were the only ones included in our present analysis. For the remainder of the manuscript, higher quality diet refers to aHEI-2010 diet scores above the lowest quintile.

Similar to the standardization of diet data, physical activity data were harmonized across the cohorts as previously reported[19]. Selfreported physical activity was assessed by questionnaire. Because each cohort used different instruments for assessing physical activity, a cohort-specific standardized z-score was calculated as the individual value minus the cohort-specific mean divided by the cohort-specific standard deviation. A participants' physical activity value was calculated as the number of minutes of moderate and vigorous intensity physical activity per week. The participant's z-score represented the number of standard deviations away from the cohort-specific mean.

Participants were stratified by body mass index (BMI) categories. BMI was calculated using the participant's weight in kilograms (kg) divided by the square of their height in meters (m). "Normal" BMI was defined as 18.5 to 24.9 kg/m<sup>2</sup>, "overweight" as 25.0 to 29.9 kg/m<sup>2</sup>, and "obese"  $\geq$  30.0 kg/m<sup>2</sup>.

## 2.3. Outcomes

The primary outcome was incident CVD defined as the composite incident event of fatal and nonfatal coronary heart disease, stroke, heart failure, and CVD death from other causes. Cohorts that were included used similar ascertainment and adjudication criteria for CVD and mortality events. Adjudication criteria included International Classification of Diseases codes (versions 8, 9, or 10); diagnostic procedures; review of medical records, autopsy data, or both. Methods for adjudication have been described in ARIC, CARDIA, FHS, FOS, MESA, and the LRPP [10]<sup>,</sup> [12]<sup>,</sup> [14–16]<sup>,</sup> [20]. The most recent follow-up ended on August 31, 2016. The last year of each individual cohort follow-up is listed in Supplemental Table 1.

## 2.4. Statistical Analysis

aHEI-2010 scores were ranked within each cohort and participants were divided into quintiles. Participants in the 0th to 20th percentile (Q1) were in the quintile with the lowest aHEI-2010 scores and thus had the worst diet as measured by the aHEI-2010, while participants in the 81st to 100th percentile (Q5) had the highest aHEI-2010 scores and thus the best diets.

Baseline characteristics were compared according to diet score quintiles using general linear models for continuous variables and cross-tabulations for categorical variables. Multivariable Cox regression models were used to estimate adjusted hazard ratios (aHR) stratified by BMI categories and sex. The proportional hazard assumption was checked and confirmed prior to analysis. The lowest quintile (Q1) aHEI-2010 group (representing poorest diet quality) was used as the reference. The Cox regression models were adjusted for total caloric intake, age, race, education, smoking status, drinking status, and level of physical activity. The interaction between diet quality and BMI category was calculated. Results were reported as fully adjusted hazard ratios (95% confidence interval) and stratified by sex and race. All analyses were performed using SAS 9.4. A 2-tailed p < 0.05 was considered statistically significant.

## 3. Results

A total of 30,219 participants were included in our study. The mean age was  $53.5 \pm 16.3$  years, 16,706 (55.3%) participants were female, and 7203 (23.8%) participants were Black (Table 1). Higher aHEI-2010 quintiles were significantly associated with less percentage of blacks, older age, female sex, greater level of education, lower percentage of current smokers, greater level of physical activity, lower BMI, lower lipid levels, and higher prevalence of statin use (p < 0.01, Table 1). Supplemental Figure 1 shows mean values and 95% confidence intervals of BMI, SBP, fasting glucose and total cholesterol by aHEI-2010 quintiles after multivariable adjustment. Higher aHEI-2010 quintiles were significantly associated with lower mean BMI (male p < 0.001; female p < 0.001) and SBP (male p = 0.004, female p < 0.001). No significant differences were observed in fasting glucose among females (p = 0.30) or total cholesterol (male p = 0.71; female p = 0.89).

During a median follow-up of 16.2 years (IQR 13.5 – 23.3; maximum 32.1), there were a total of 7021 CVD events. We observed a significant interaction between diet quality quintiles and BMI category (p = 0.0009). Among participants with normal weight, the quintile with the highest aHEI-2010 scores (highest diet quality) had 7.1 events per 1000 participant-years (PY) compared to 11.5 events per 1000 PY in the lowest aHEI-2010 quintile. In participants who were overweight, the highest quintile group had an event rate of 13.2 events per 1000 PY compared to 17.3 events per 1000 PY in the lowest quintile group. For participants with obesity, the quintile with the highest diet qualities had 18.2 events per 1000 PY compared to 16.8 events per 1000 PY in the lowest quintile group (Supplemental Figure 2).

In fully adjusted Cox regression analysis, the highest diet quality quintile was significantly associated with lower risk of cardiovascular events when compared to the lowest diet quality quintile in participants who were normal weight (adjusted hazard ratio [aHR] 0.79; 95% confidence interval [CI] 0.68 - 0.92) and overweight (aHR 0.84; 95% CI 0.75 - 0.95) but not in participants with obesity (aHR 1.17; 95% CI 1.01 - 1.36) (Fig. 1). A similar pattern of associations was observed when stratified by sex (Fig. 1). When stratified by race, Black participants did not have any significant association between diet quality and cardiovascular events when stratified by BMI categories (Supplemental Figure 3).

## 4. Discussion

While diet quality is known to be associated with lower BMI, which our results also support, data are sparse on the associations of diet quality with incident CVD within and across BMI strata[21]. To our knowl-

#### Table 1

Baseline demographics data of study population by aHEI-2010 quintiles. Q1 represents the quintile with the lowest diet qualities, while Q5 is the quintile with the highest quality diets per aHEI-2010 score.

		Diet Quality Quintiles					
		Q1 (n = 6041)	Q2 (n = 6045)	Q3 (n = 6045)	Q4 (n = 6045)	Q5 (n = 6043)	p-trend
Demographics	Age (years)	52.4 (14.7)	53.3 (14.7)	53.6 (14.7)	54.1 (14.7)	54.3 (14.5)	< 0.001
	Female sex	2568 (42.5%)	3103 (51.3%)	3409 (56.4%)	3718 (61.5%)	3908 (64.7%)	< 0.001
	Self-reported Black race	1870 (31.0%)	1669 (27.6%)	1535 (25.4%)	1207 (20.0%)	922 (15.3%)	< 0.001
	Education						
	< High School	1500 (25.0%)	1352 (22.5%)	1087 (18.1%)	958 (16.0%)	664 (11.0%)	< 0.001
	High School	1961 (32.6%)	1851 (30.8%)	1773 (29.5%)	1620 (27.0%)	1429 (23.8%)	
	≥ College	2550 (42.2%)	2815 (46.8%)	3158 (52.4%)	3423 (57.0%)	3920 (65.2%)	
Lifestyle	Alcohol use	2465 (40.9%)	2764 (45.8%)	3072 (50.2%)	3340 (55.3%)	3861 (64.0%)	< 0.001
	Smoking status						
	Never	2582 (42.7%)	2891 (47.8%)	3007 (49.7%)	3040 (50.3%)	2982 (49.4%)	< 0.001
	Former	1672 (27.7%)	1726 (28.6%)	1762 (29.2%)	1949 (32.2%)	2207 (36.5%)	
	Current	1787 (29.6%)	1428 (23.6%)	1276 (21.1%)	1056 (17.5%)	854 (14.1%)	
	Physical activity (z-score)	-0.13 (0.98)	-0.08 (0.95)	-0.04 (0.99)	0.07 (1.00)	0.26 (1.04)	< 0.001
Clinical Factors	Body mass index (kg/m <sup>2</sup> )	27.8 (5.4)	27.5 (5.2)	27.4 (5.2)	27.0 (5.1)	26.2 (4.6)	< 0.001
	Systolic blood pressure (mmHg)	123.7 (19.5)	123.7 (20.1)	123.0 (19.4)	122.9 (20.2)	121.0 (19.6)	< 0.001
	Diastolic blood pressure (mmHg)	73.3 (10.9)	72.9 (11.0)	72.6 (10.5)	72.0 (10.6)	70.9 (10.2)	< 0.001
	Anti-hypertensive use	1446 (24.0%)	1565 (25.9%)	1587 (26.3%)	1607 (26.6%)	1484 (24.6%)	0.002
	Fasting Glucose (mg/dL)	100.8 (30.7)	101.4 (32.9)	101.4 (31.6)	100.3 (31.7)	98.3 (27.6)	< 0.001
	Diabetes	485 (8.1%)	556 (9.2%)	645 (10.7%)	531 (8.8%)	420 (7.0%)	< 0.001
	Total Cholesterol (mg/dL)	202.8 (41.3)	204.2 (39.9)	204.5 (40.1)	205.3 (41.0)	204.9 (40.9)	0.011
	High density lipoprotein (mg/dL)	48.8 (14.7)	50.7 (15.1)	51.8 (15.4)	53.4 (15.9)	55.3 (16.6)	< 0.001
	Non high density lipoprotein (mg/dL)	154.0 (42.4)	153.5 (41.0)	152.7 (41.2)	151.9 (42.3)	149.6 (42.5)	< 0.001
	Lipid lowering medication use	243 (4.1%)	269 (4.5%)	343 (5.7%)	414 (6.9%)	403 (6.7%)	< 0.001
	aHEI-2010 score	34.6 (8.5)	43.3 (8.0)	49.0 (7.9)	54.8 (7.3)	64.1 (10.0)	

#### Overall Men Vomen

BMI	aHEI	Ν	Events	Event Rate	
Normal	Q1	2023	443	11.4	•
18.5 - 24.9	Q2	2078	420	10.6	
	Q3	2151	370	8.7	
	Q4	2351	365	7.9	
p = 0.002	Q5	2738	390	7.1	
Overweight	Q1	2295	646	17.3	
25.0 - 29.9	Q2	2355	614	15.2	
	Q3	2330	557	14	- <b>-</b>
	Q4	2311	553	13.8	
p = 0.007	Q5	2222	508	13.2	
Obese	Q1	1714	466	16.8	•
≥ 30	Q2	1612	483	18.8	
	Q3	1564	470	18.1	
	Q4	1383	417	18.7	
p = 0.037	Q5	1083	319	18.2	
					0.71 1.75 Adjusted Hazard Ratio

**Fig. 1.** Forest plot of incident cardiovascular disease adjusted hazard ratios stratified by aHEI-2010 quintiles and BMI groups. Numbers in the table are for the overall cohort. Men (purple circle) and women (orange diamond) stratification are shown for adjusted hazard ratios. Hazard ratios were calculated using the lowest quintile aHEI-2010 group as the reference centered at 1. p-values are comparison of Q5 with Q1. Results are adjusted for age, race, level of education, smoking status, alcohol use, physical activity level, and total caloric intake. Event rates reported as per 1000 participant-years. aHR, adjusted hazard ratio; CI, confidence interval; ref, reference value.

edge, this is one of the first large, diverse cohort studies to examine the independent association between diet quality and CVD incidence stratified by BMI. Among 30,219 participants pooled across 6 prospective cohorts in the United States with a median follow-up of 16.2 years, higher diet quality as measured by aHEI-2010 score was significantly associated with a lower risk of incident CVD even in participants who were normal weight and overweight, but not in those who were obese at the time of dietary assessment (on average in middle age). While no significant association was seen when stratified by race, there was a nonsignificant trend towards higher diet quintiles and lower incident CVD in Black participants with normal BMI (Supplemental Figure 3).

Interestingly, an inverse relationship was observed in men with obesity where the highest aHEI-2010 score quintiles (Q4 and Q5) were associated with higher incidence of cardiovascular disease. We propose 3 hypotheses why this relationship is observed. First, the fact that obesity is a strong, known risk factor for CVD suggests a causal relationship in the observed mitigation of diet quality on risk of CVD in participants with obesity. Second, obesity and other cardiovascular risk factors, such as hypertension and diabetes, may have increased this cohort's risk to a degree where improvement of diet quality had minimal effect. In fact, when adjusted for clinical risk factors such as hypertension, diabetes, and hyperlipidemia, the significantly higher incidence of cardiovascular disease in participants with obesity was not observed (Supplemental Figure 4). Third, those with obesity in the higher diet qualities may have improved their diets prior to enrollment in their studies due to their higher baseline risk, particularly among older participants, thus possibly leading to reverse causation or protopathic bias. It is worth noting that we chose not to adjust for clinical risk factors such as hypertension, diabetes, and hyperlipidemia in our current analysis due to risk of overadjustment as diet quality plays a role in the development of those risk factors.

It is worth noting that in the current cohort study, only conclusions regarding associations can be made and the results cannot be used to infer causality. As such, despite these findings, we would like to emphasize that significant evidence exists that consuming a high-quality diet is an important strategy for decreasing health risks from chronic conditions such as diabetes, hypertension, and metabolic syndrome in individuals with obesity[22–24]. A recent prospective study of Spanish

adults with overweight and obese BMIs found that even after 12 months of follow-up, participants in the intensive weight-loss intervention arm of the trial improved their carbohydrate quality index and their intermediate markers of CVD risk such as weight, waist circumference, blood pressure, blood glucose, triglycerides, and HDL cholesterol[25]. However, further work examining the effects of dietary changes on risk of CVD in individuals with obesity outside of a trial setting are needed.

A secondary finding worth noting is that individuals with better diet qualities were more likely to have greater levels of education, greater physical activity, and less likely to be current smokers (Table 1). This is consistent with a number of reports that healthy behaviors tend to cluster together, and that socioeconomic status plays a large role in cardiovascular risk factors[26–29]. One limitation is the potential for residual confounding in the present analysis. While our study was not designed to examine the role of behavior clustering and socioeconomic status, these associations should continue to be explored as they likely contribute to ongoing health disparities.

It is worth noting that there are other dietary models, such as the Dietary Approaches to Stop Hypertension (DASH) and the Mediterranean Diet, which have been shown to reduce blood pressure and major cardiovascular events in high risk individuals in randomized control trials[30].<sup>7</sup> [31] We chose to use the aHEI-2010 because it was based on dietary guidelines for Americans which is most relevant to our study sample of US adults[18]. Additionally, aHEI was specifically curated to represent dietary patterns which were associated with lower risk of chronic disease including CVD and includes foods and nutrients not covered by other diets such as the DASH diet[18].<sup>,</sup> [30] Since analysis of our study, the aHEI developed a newer scoring system in 2015 and the American Heart Association has advocated for the adoption of DASH, the Mediterranean Diet, and the US Department of Agriculture dietary food patterns as guidelines for reducing co-morbid conditions in cardiovascular disease [32].<sup>7</sup> [33] The dietary assessments included in this study were prior to newer guideline recommendations and our study was not designed to assess dietary changes over time. Further work into the risk reduction of cardiovascular events of newer dietary recommendations on a contemporary cohorts would be of particular interest. Finally, underweight participants, defined as BMI < 18.5, were excluded from analysis because there were fewer participants who were underweight and they experienced significantly higher rates of CVD events. This is likely because being underweight is a clinical marker of advanced disease states such as chronic obstructive pulmonary disease or metastatic cancer.

There are several strengths to the present study. This longitudinal study queried diet data for a large number of participants (n = 30,219) with long follow-up (median 16.2 years) to gain insight into the association of diet quality with future cardiovascular events. Additionally, we had a diverse population with a significant number of female (55.3%) and Black participants (23.8%), two often under-represented groups in cardiovascular research. Lastly, the LRPP pools together individual participant level data from each included cohort. This degree of individual levels pooled analyses allows for greater harmonization, standardization, and covariate adjustment of data across cohorts as compared to traditional meta-analyses which rely on limited data and variables published in manuscripts[34].

There are several notable limitations. First, only baseline diet data for each cohort were harmonized for this study. It is unclear whether individuals remained in the same aHEI-2010 quintile throughout the study period and thus our findings do not reflect changes in diet quality over an individual's lifetime. Second, appropriate interpretation of the study findings requires consideration of measurement error for selfreported diet data. Additionally, the assigned weighting of qualitative portion sizes in the MESA cohort may not accurately reflect relationships between real portion sizes. We attempted to mitigate this through the use of cohort-specific aHEI-2010 rankings. Third, except for the two Framingham cohorts, all cohorts used different dietary assessment tools which may have introduced heterogeneity. We attempted to minimize this heterogeneity by scoring each individuals' dietary intake using a standardized scoring algorithm (Supplemental Table 2). Additionally, because cohorts used a different dietary assessments, we attempted to limit unfair comparisons between cohorts by performing aHEI-2010 quintile ranking within each cohort instead of by the overall population[17]. Finally, these studies are observational and cannot establish causality. Additionally, there remains a potential for residual confounding given the various associations seen with higher aHEI-2010 scores as above.

## 5. Conclusion

We observed that higher diet quality is associated with lower risk of incident cardiovascular events among individuals who have BMIs in the normal weight and overweight categories but not in individuals with BMIs in the obese category, especially among men. On a societal level, improving diet quality is a safe intervention with profound public health implications for the entire population. From a clinical perspective, counseling of a healthy diet should be initiated early in life and sustained regardless of weight category.

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## **Declaration of Competing Interests**

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

### CRediT authorship contribution statement

Nathan W. Kong: Conceptualization, Writing – original draft, Writing – review & editing, Visualization. Hongyan Ning: Methodology, Software, Formal analysis, Writing – review & editing. Victor W. Zhong: Software, Formal analysis, Writing – review & editing. Amanda Paluch: Software, Formal analysis, Writing – review & editing. John T. Wilkins: Investigation, Writing – review & editing, Funding acquisition. Donald Lloyd-Jones: Investigation, Writing – review & editing, Funding acquisition. Norrina B. Allen: Conceptualization, Methodology, Writing – review & editing, Supervision.

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## Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ajpc.2021.100298.

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