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Relationships of the Mediterranean dietary pattern with insulin resistance and diabetes incidence in the Multi-Ethnic Study of Atherosclerosis (MESA)

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Abstract

Type 2 diabetes (T2D) is a highly prevalent but preventable disorder. We assessed the association between an *a priori* Mediterranean diet (MeDiet) score and fasting glucose and insulin at baseline and incident T2D after a 6-year follow-up in the Multi-Ethnic Study of Atherosclerosis. Dietary intake was measured at baseline using a 127-item FFQ in 5390 men and women aged 45–84 years free of prevalent diabetes and clinical CVD. A MeDiet score was created based on the intake of ten food components: vegetables; whole grains; nuts; legumes; fruits; ratio of monounsaturated:saturated fat; red and processed meat; dairy products; fish; alcohol. Multivariable linear and proportional hazards models were used to estimate the association of the MeDiet, categorised in quintiles, with baseline insulin and glucose, and incident diabetes, respectively. The models were adjusted for demographic, physiological and behavioural characteristics. After multivariable adjustment, individuals with a higher MeDiet score had lower baseline mean insulin levels (Q1: 5·8 (95 % CI 5·6, 6·0) μmol/l; Q5: 4·8 (95 % CI 4·6, 5·0) μmol/l; *P* for trend $<0{\cdot}0001$). A higher MeDiet score was also associated with significantly lower glucose levels after basic adjustment, but was attenuated after adjustment for waist circumference. During the follow-up, 412 incident diabetes events accrued. The MeDiet was not significantly related to the risk of incident diabetes (*P* for trend=0·64). In summary, greater consistency with a Mediterranean-style diet, reflected by a higher *a priori* MeDiet score, was cross-sectionally associated with lower insulin levels among non-diabetics, and with lower blood glucose before adjustment for obesity, but not with a lower incidence of diabetes.

Key words: Mediterranean diet: Insulin: Glucose: Diabetes: Multi-Ethnic Study of Atherosclerosis (MESA)

Diabetes affects approximately twenty-four million people in the USA, 8 % of the population, and is currently the seventh leading cause of death. It has been projected that the prevalence of diabetes will reach 26 % by 2050[1]. Accounting for about 95 % of all diagnosed cases in the USA, type 2 diabetes (T2D) results in complications such as kidney failure, amputations and blindness, affecting the quality of life[2]. Management of the disease also poses a huge medical burden and economic impact, making it a current public health priority. T2D can, however, be prevented through healthy diets, other lifestyle modifications such as weight loss and the use of medication[3].

The Mediterranean diet (MeDiet) is the traditional diet of people living in olive-growing regions bordering the Mediterranean Sea. It is of public health interest due to the observation that adults living in these areas have historically had one of the lowest incidences of chronic diseases in the world and one of the highest life expectancies[4]. This diet is characterised by a high consumption of whole grains, olive oil, legumes, vegetables, fruits and cereals, moderate to high consumption of fish and moderate to low consumption of meat and meat products and milk and dairy products. Alcohol in the form of wine is often consumed at meals[5]. Extensive research has demonstrated a beneficial effect of specific dietary components of the MeDiet on weight loss, normalising insulin resistance, and the risk of developing T2D and CVD[5–7]. The MeDiet is widely viewed as 'health promoting', both among the scientific community and among the general public. Possible mechanisms by which intake of the MeDiet may be associated with lower diabetes risk include fibre increasing satiety through prolonged mastication and antioxidants reducing the stress of β-cell dysfunction and insulin

Abbreviations: IFG, impaired fasting glucose; MeDiet, Mediterranean diet; MESA, Multi-Ethnic Study of Atherosclerosis; T2D, type 2 diabetes.

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resistance[8]. Relationships of the MeDiet to disease risk may also be mediated through the anti-inflammatory effects of vitamins, minerals, antioxidants and unsaturated fat – particularly olive oil – present in high levels in the MeDiet[5,7,9,10].

There is limited evidence of the association between insulin resistance – as a precursor of diabetes – and the MeDiet in non-diabetic individuals. Additionally, little research has investigated whether racial/ethnic heterogeneity exists in the relationship between the intake of a Mediterranean-style diet and the incidence of diabetes and the onset of insulin resistance. We hypothesised that in a community-based sample free of diabetes and CVD, a high conformity to the Mediterranean-style diet would be associated cross-sectionally with lower insulin resistance and prospectively with a reduced risk of T2D incidence. Our MeDiet index was created *a priori*, and focused on those food groups commonly attributed to the Mediterranean cuisine, i.e. vegetables, whole grains, nuts, legumes, fruits, MUFA:SFA ratio and fish.

Methods

Study population

The Multi-Ethnic Study of Atherosclerosis (MESA) is a prospective population-based cohort study of 6814 persons aged 45–84 years who self-identified as Hispanic, non-Hispanic Caucasian, African-American and Asian Chinese[11]. The study was initiated in July 2000 to determine the characteristics associated with the prevalence and progression of subclinical CVD to clinically overt CVD, as well as to investigate demographic differences and identify risk factors for CVD incidence. Baseline information was collected from enrollees, all of whom were free from clinical CVD, at six US field centres: Chicago, IL; Los Angeles County, CA; New York, NY; Forsyth County, NC; St Paul, MN and Baltimore, MD. A detailed study protocol and inclusion criteria can be found at www.mesa-nhlbi.org. The present study was conducted according to the guidelines laid down in the Declaration of Helsinki, and all procedures involving human subjects were approved by the Institutional Review Boards from each study centre. All participants gave written informed consent.

Dietary pattern assessment

At baseline, a 127-item FFQ was used to assess usual dietary intake of participants over the past year. For each questionnaire item, participants were asked to report their frequency of consumption of various foods from among nine categories, ranging from rarely or never to two or more servings/d (six or more servings/d for beverages), and also their serving size as either small, medium or large. Servings per d were calculated from these categories. The questionnaire was patterned after the FFQ used in the Insulin Resistance Atherosclerosis Study, which has been validated in non-Hispanic white, African-American and Hispanic persons[12].

To ascertain conformity to a Mediterranean-style diet, a ten-point *a priori* alternate MeDiet score was created. The MeDiet score was adapted to the US population from a scoring system modelled for Greek populations and focuses on higher consumption of plant foods, monounsaturated fat, fish and lower intake of animal products and saturated fat[6,13]. As detailed in Table 1, the score included ten food components: vegetables (excluding potatoes); whole grains; nuts; legumes; fruits; ratio of monounsaturated:saturated fat; red and processed meat; whole-fat dairy products; fish; alcohol[14]. Participants with intakes above the median intake of traditional foods in the MeDiet (i.e. vegetables, whole grains, nuts, legumes, fruits, MUFA:SFA ratio, fish) received 1 point, while those below the median received 0 points. For potentially detrimental foods inversely associated with the MeDiet (i.e. red/processed meats, whole-fat dairy products), those with intakes below the median received 1 point; otherwise, they received 0 points. For example, red or processed meat below the median intake received 1 point. Alcohol intake received 1 point if consumed in moderate amounts (5–15 g/d) and 0 otherwise (<5 and >15 g/d). The points were then summed. The final MeDiet score ranged from 0 to 10, with a higher score indicating a closer resemblance to the MeDiet.

Outcome ascertainment

Insulin resistance was cross-sectionally characterised using mean baseline fasting glucose and fasting serum insulin

Table 1. Food group components of the ten-point Mediterranean diet score: the Multi-Ethnic Study of Atherosclerosis (2000–2)

Food group	Foods included	Criteria for 1 point*
Vegetables	All vegetables (cruciferous vegetables, dark yellow vegetables, green leafy vegetables, other vegetables) except potatoes	Greater than median intake
Legumes	Legumes, soya	Greater than median intake
Fruit	Fruits, fruit juice, avocado, tomato	Greater than median intake
Nuts	Seeds, nuts	Greater than median intake
Whole grains	All whole-grain products	Greater than median intake
Fish	All fish	Greater than median intake
Red meat	Red and processed meats	Less than median intake
Ratio of monounsaturated: saturated fat	–	Greater than median intake
Alcohol	Total alcohol (beer, liquor, wine)	Moderate intake (>5 and <15 g/d)
Dairy products	Whole milk, high-fat cheeses and sauces	Less than median intake

*0 points if these criteria are not met.

levels among non-diabetics. Fasting serum glucose was measured at each examination using the thin-film adaptation of the glucose oxidase method on the Vitros analyser (Johnson & Johnson Clinical Diagnostics, Inc.). To ensure consistency of the fasting serum glucose assay over the examinations, 200 samples from each of the four examinations were reanalysed over a short time period to recalibrate the original observations. Fasting serum insulin levels were determined by a RIA method using the Linco Human Insulin-Specific RIA Kit (Linco Research, Inc.). These assays were conducted at the Collaborative Studies Clinical Laboratory at Fairview University Medical Center[15–17].

Table 2. Baseline characteristics* by quintiles of the Mediterranean dietary score: the Multi-Ethnic Study of Atherosclerosis (2000–2)
(Mean values and standard deviations; number of participants and percentages)

Quintile†...	1		2		3		4		5	
MeDiet score range...	0–3		4		5		6		7–10	
n...	1240		967		1051		932		1200	
	n	%	*n*	%	*n*	%	*n*	%	*n*	%
Demographics										
Age (years)										
Mean	60		62		62		63		63	
SD	10·3		10·2		10·3		10·2		10·3	
Women	676	54·5	522	54·0	552	52·5	505	54·2	629	52·4
Racial/ethnic group										
White	547	44·1	396	41·0	425	40·4	377	40·5	558	46·5
Chinese	68	5·5	99	10·2	163	15·5	165	17·7	180	15·0
African-American	293	23·6	243	25·1	244	23·2	230	24·7	305	25·4
Hispanic	332	26·8	229	23·7	219	20·8	160	17·2	157	13·1
Formal education										
Less than high school diploma	249	20·2	193	20·0	182	17·3	132	14·2	122	10·2
High school or some college	628	50·8	484	50·1	464	44·2	132	44·7	471	39·3
College diploma	359	29·0	289	29·9	405	38·5	132	41·1	606	50·5
Gross family income										
< $20 000	277	23·0	222	24·1	249	24·5	194	21·4	213	18·3
$20 000– < $50 000	460	38·2	379	41·1	338	33·2	324	35·8	360	30·9
≥ $50 000	466	38·8	322	34·9	431	42·3	388	42·8	592	50·8
BMI (kg/m^2)										
Mean	28·9		28·0		27·9		27·5		27·1	
SD	5·7		5·2		5·3		5·2		4·8	
Waist circumference (cm)										
Mean	99·2		97·2		97·0		95·9		94·9	
SD	14·8		13·8		13·8		13·9		13·2	
Behavioural										
Current smoking	236	19·1	136	14·1	122	11·6	83	8·8	90	7·5
Pack-years of cigarette smoking (years)										
Mean	14·6		11·6		10·7		8·2		9·7	
SD	30·1		20·5		21·6		15·1		18·5	
Physical activity (MET-min/week)										
Mean	3495		2921		2987		2934		2806	
SD	4114		3702		3888		3889		3646	
Physiological										
SBP (mmHg)										
Mean	124		127		125		126		126	
SD	22		21		21		21		21	
DBP (mmHg)										
Mean	72		73		72		72		72	
SD	10		10		10		10		10	
TAG (mg/l)										
Mean	1310		1290		1320		1230		1180	
SD	750		760		800		650		660	
LDL-cholesterol (mg/l)										
Mean	1200		1180		1160		1180		1170	
SD	310		320		300		300		310	
HDL-cholesterol (mg/l)										
Mean	509		513		512		523		530	
SD	148		146		148		158		153	
Hypertensive medication use	318	25·6	293	30·3	324	30·8	292	31·3	365	30·4
Statins use	139	11·2	133	13·7	142	13·5	122	13·1	179	14·9

MeDiet, Mediterranean diet; MET, metabolic equivalent; systolic blood pressure; DBP, diastolic blood pressure.
* Participants with prevalent diabetes were excluded.
† Higher quintile represents closer conformity to the MeDiet.

To determine incident diabetes, we excluded from the analyses individuals with diabetes at baseline, defined as fasting blood glucose ≥7·0 mmol/l (1260 mg/l), self-reported diabetes or using hypoglycaemic drugs. During follow-up examinations 2 (2002–3), 3 (2004–5) and 4 (2005–7), participants without diabetes at baseline who met any of the above three criteria were considered to have incident T2D. Person-years were accrued from baseline until the date of the examination at which incident diabetes was identified, loss to follow-up or the date of examination 4.

Covariate assessment

Demographic data were obtained during the baseline examination (2000–2) with a standardised questionnaire and calibrated devices. Participants self-reported their racial/ethnic groups and were characterised as Caucasian, Chinese, African-American and Hispanic. The annual gross family income was categorised as <$20 000, $20 000– < $50 000 and ≥$50 000, and the level of formal education was classified as less than high school diploma, high school or some college and college diploma. Height was measured with a stadiometer with a level bubble (Accu-Hite Measuring device; Seca GmbH & Company KG) and weight with a Detecto platform balance scale (Titus Home Health Care). BMI was calculated as weight (in kg) divided by the square of height (in m^2). Waist circumference (in cm) was measured at the level of the umbilicus. Resting seated blood pressure was measured three times using a Dinamap model Pro 100 automated oscillometric sphygmomanometer (Critikon), and the average of the last two measurements was used in the analysis.

Additional variables such as use of hypertensive medication, use of statins (3-hydroxy-3-methyl-glutaryl (HMG)-CoA reductase inhibitors), cigarette smoking status and time spent in moderate to vigorous exercise (metabolic equivalent (MET)-min/week) were obtained from a combination of self-administered and interviewer-administered questionnaires. Pack-years of smoking, defined as number of years smoking times packs per d (cigarettes per d divided by 20), were then calculated[15,18–20].

Statistical analyses

All analyses were performed using SAS software (version 9.2; SAS Institute). Of the 6814 MESA participants, we excluded those with prevalent diabetes (*n* 859), missing values (*n* 24) and people with unrealistic dietary intake (*n* 541). Unrealistic dietary intake was defined as energy intake of <2092 or >20 920 kJ/d (<500 or >5000 kcal/d). The present final analytic sample included 5390 individuals.

Cross-sectional demographic, behavioural and physiological characteristics across quintiles of the MeDiet score were quantified using means and proportions. We used multivariable linear regression to assess the association of the MeDiet with insulin resistance. Separate analyses were conducted for fasting glucose and insulin at baseline across MeDiet quintiles. After checking for normality of these outcomes, serum insulin was found to be skewed and was therefore log-transformed for multivariate analyses. The adjusted mean values were then back-transformed to obtain geometric means. Adjusted means at each MeDiet quintile were obtained by entering the MeDiet quintiles into the models as indicator variables. To test the linear trend across the quintiles of the MeDiet score, quintiles were entered into the models as continuous variables.

We used three multivariable models in the present analysis. The first model (model 1) adjusted for age, sex, race/ethnicity and study site. Model 2 adjusted for model 1 variables plus educational level, family income, physical activity, smoking status and total energy intake. Further, to assess the effect of body adiposity and how this might mediate the association of the MeDiet and the outcomes, waist circumference was included in the final model (model 3). In sensitivity analyses, we explored substituting BMI for waist circumference.

Cox proportional hazards regression models were used to estimate the hazard ratios of developing T2D by MeDiet quintiles. The adjustment approach was similar to the cross-sectional analysis, with quintile 1 as the reference for the Cox regression model. We further tested whether there were interactions by sex and race/ethnicity in the relationship between the MeDiet and the outcomes by including cross-product terms in our models. In sensitivity analyses, we evaluated the risk of incident impaired fasting glucose (IFG) or diabetes in a subset free of IFG and diabetes at baseline.

Results

The 5390 participants in the present analytic sample were on average 62 (SD 10) years old and 54 % were female. The racial/ethnic distribution was as follows: 43 % Caucasian; 13 % Chinese; 24 % African-American; 20 % Hispanic. The average MeDiet score was 5·0 (SD 1·9) on a 0–10-point scale within the study population. Participants who had higher MeDiet scores, indicating a high conformity to the MeDiet, were more likely to be female, more educated, have higher incomes, a smaller waist circumference and be non-smokers (Table 2). In this population of non-diabetics, the mean glucose level was 895 mg/l, and the geometric mean insulin level was 5·25 μmol/l. Furthermore, 15·7 % (*n* 841) of the analytic sample had IFG, as defined by fasting glucose levels of 1000–1250 mg/l.

Participants with a higher MeDiet score had lower insulin levels after model 2 adjustments (Q1: 5·8 (95 % CI 5·6, 6·0) μmol/l; Q5: 4·8 (95 % CI 4·6, 5·0) μmol/l; *P* for trend <0·0001; Table 3). The results were similar to model 1, and this relationship remained significant in model 3, which was further adjusted for waist circumference (*P* for trend <0·0001). Upon stratification by sex, the association among men remained significant across all models, while among women, the association was attenuated after adjustment for waist circumference (model 3, *P* for trend=0·11). After model 2 adjustments, mean fasting glucose was also lower for individuals in MeDiet quintile 5 (890 (95 % CI 884, 896) mg/l) relative to those in MedDiet quintile 1 (903 (95 % CI 897, 909) mg/l) (*P* for trend=0·009). The relationship,

Table 3. Glucose and insulin levels by the Mediterranean dietary score quintiles: the Multi-Ethnic Study of Atherosclerosis (2000–2)

(Adjusted mean values and 95 % confidence intervals)

	1		2		3		4		5			
Quintile*	Mean	95 % CI	Mean	95 % CI	Mean	95 % CI	Mean	95 % CI	Mean	95 % CI	β for one quintile increase	*P* for trend
Total population												
Glucose (mg/l)												
Model 1†	903	898, 909	891	885, 897	896	890, 902	892	886, 899	890	884, 896	−0·27	0·005
Model 2‡	903	897, 909	889	882, 895	896	890, 902	892	885, 898	890	884, 896	−0·26	0·009
Model 3§	899	893, 904	889	883, 895	895	889, 901	893	887, 900	894	888, 899	−0·07	0·450
Insulin (μmol/l)‖												
Model 1†	5·7	5·5, 5·9	5·3	5·1, 5·5	5·3	5·1, 5·5	5·1	4·9, 5·3	4·8	4·7, 5·0	−0·04	<0·0001
Model 2‡	5·8	5·6, 6·0	5·3	5·1, 5·5	5·3	5·1, 5·5	5·0	4·8, 5·2	4·8	4·6, 5·0	−0·04	<0·0001
Model 3§	5·5	5·4, 5·7	5·3	5·1, 5·5	5·3	5·1, 5·4	5·1	4·9, 5·3	5·0	4·9, 5·2	−0·02	<0·0001
Males												
Glucose (mg/l)												
Model 1†	927	918, 935	910	900, 919	911	902, 920	911	901, 921	906	897, 914	−0·42	0·003
Model 2‡	927	918, 936	907	898, 917	913	904, 922	911	901, 920	905	896, 913	−0·43	0·004
Model 3§	922	914, 931	907	898, 916	913	904, 922	913	903, 922	908	899, 916	−0·26	0·070
Insulin (μmol/l)‖												
Model 1†	6·1	5·8, 6·4	5·3	5·0, 5·6	5·2	4·9, 5·5	4·9	4·7, 5·2	5·0	4·7, 5·2	−0·05	<0·0001
Model 2‡	6·2	5·9, 6·5	5·3	5·0, 5·7	5·3	5·0, 5·6	4·9	4·6, 5·2	4·9	4·6, 5·1	−0·06	<0·0001
Model 3§	5·8	5·6, 6·1	5·3	5·1, 5·6	5·3	5·0, 5·5	5·0	4·8, 5·3	5·1	4·9, 5·3	−0·03	<0·0001
Females												
Glucose (mg/l)												
Model 1†	884	876, 891	875	866, 883	883	875, 892	876	867, 885	877	869, 885	−0·13	0·32
Model 2‡	883	875, 891	872	863, 881	881	873, 890	875	866, 884	877	869, 885	−0·10	0·48
Model 3§	878	871, 886	873	865, 882	880	872, 888	876	867, 885	881	874, 889	0·09	0·50
Insulin (μmol/l)‖												
Model 1†	5·4	52, 5·7	5·3	5·0, 5·6	5·4	5·1, 5·6	5·2	4·9, 5·5	4·7	4·5, 5·0	−0·03	0·0002
Model 2‡	5·4	5·2, 5·7	5·2	5·0, 5·5	5·3	5·1, 5·6	5·2	4·9, 5·4	4·8	4·6, 5·0	−0·03	0·0005
Model 3§	5·2	5·0, 5·4	5·3	5·1, 5·5	5·3	5·0, 5·5	5·2	5·0, 5·4	5·0	4·8, 5·2	−0·01	0·11

* Higher quintile represents closer conformity to the Mediterranean diet.

† Model 1 adjusted for age, sex, race/ethnicity and study site.

‡ Model 2 adjusted for model 1 + educational level, family income, smoking status, physical activity and total energy intake.

§ Model 3 adjusted for model 2 + waist circumference.

‖ Values for quintiles 1–5 are geometric means. β for one quintile increase in the Mediterranean diet score are presented on the log scale. The log-scale β multiplied by 100 gives the percentage change per one quintile increase in the Mediterranean diet score. For example, using model 1 and the total population, each one quintile increase in the Mediterranean diet score is associated with a 4 % lower insulin level.

Table 4. Hazard ratios (HR) of type 2 diabetes across quintiles of the Mediterranean dietary score: the Multi-Ethnic Study of Atherosclerosis (2000–7)

(Hazard ratios and 95 % confidence intervals)

Quintiles*...	1	2		3		4		5		HR for one quintile increase		*P* for trend
	HR	HR	95 % CI	HR	95 % CI	HR	95 % CI	HR	95 % CI	HR	95 % CI	
Total population												
Events (*n*)	99	73		83		68		89				
Person-years	4936	3886		4230		3702		5013				
Incidence rate†	20·1	18·8		19·6		18·4		17·8				
Model 1‡	1 (reference)	0·93	0·69, 1·26	1·00	0·75, 1·35	0·96	0·70, 1·31	0·93	0·69, 1·25	0·99	0·92, 1·06	0·71
Model 2§	1 (reference)	0·88	0·65, 1·20	0·97	0·72, 1·31	0·93	0·67, 1·28	0·91	0·67, 1·23	0·98	0·92, 1·06	0·64
Model 3‖	1 (reference)	1·01	0·74, 1·38	1·04	0·77, 1·41	1·08	0·78, 1·50	1·09	0·80, 1·49	1·02	0·95, 1·10	0·51
Males												
Events (*n*)	41	40		41		35		42				
Person-years	2281	1799		2048		1691		2350				
Incidence rate†	18·0	22·2		20·0		20·7		17·9				
Model 1‡	1 (reference)	1·19	0·77, 1·84	1·09	0·70, 1·69	1·19	0·75, 1·87	1·02	0·65, 1·58	1·00	0·91, 1·10	0·98
Model 2§	1 (reference)	1·12	0·71, 1·75	1·07	0·68, 1·66	1·08	0·67, 1·73	0·95	0·60, 1·50	0·99	0·89, 1·09	0·79
Model 3‖	1 (reference)	1·24	0·79, 1·94	1·15	0·74, 1·81	1·26	0·78, 2·04	1·11	0·70, 1·76	1·02	0·92, 1·13	0·69
Females												
Events (*n*)	58	33		42		33		47				
Person-years	2656	2087		2182		2011		2664				
Incidence rate†	21·8	15·8		19·2		16·4		17·6				
Model 1‡	1 (reference)	0·73	0·48, 1·12	0·93	0·62, 1·39	0·77	0·50, 1·18	0·86	0·58, 1·27	0·97	0·88, 1·06	0·51
Model 2§	1 (reference)	0·70	0·45, 1·09	0·88	0·58, 1·34	0·78	0·50, 1·22	0·89	0·59, 1·35	0·98	0·89, 1·08	0·70
Model 3‖	1 (reference)	0·82	0·53, 1·29	0·95	0·62, 1·45	0·92	0·59, 1·45	1·12	0·74, 1·71	1·03	0·93, 1·14	0·55

* Higher quintile represents closer conformity to the Mediterranean diet.
† Incidence per 1000 person-years.
‡ Model 1 adjusted for age, sex, race/ethnicity and study site.
§ Model 2 adjusted for model 1+educational level, family income, smoking status, physical activity and total energy intake.
‖ Model 3 adjusted for model 2 + waist circumference.

however, disappeared after adjusting for waist circumference (model 3, *P* for trend=0·45).

After 6·6 years of follow-up, 412 participants (7·6 %) developed T2D. In this study population, the MeDiet was not significantly related to the risk of T2D incidence, and this relationship was consistent across sex (Table 4) and racial/ethnic groups (results not shown for the racial/ethnic groups). The model 2 multivariable hazard ratio of T2D among those in the highest quintile of the MeDiet score *v.* the lowest quintile was 0·91 (95 % CI 0·67, 1·23, *P* for trend=0·64; Table 4).

In additional analyses, there were no significant interactions by race/ethnicity or sex in the relationship between the MeDiet and insulin levels, glucose levels or the incidence of diabetes. The results were similar when we adjusted for BMI instead of waist circumference (data not shown). Furthermore, we also evaluated the risk of incident IFG or diabetes in a subset free of IFG and diabetes at baseline. There was no evidence that the MeDiet score was associated with a lower risk of incident IFG or diabetes. The hazard ratio for one quintile change in the MeDiet score was 0·98 (95 % CI 0·94, 1·02).

Discussion

In the present population-based, multi-ethnic sample, a higher consumption of the Mediterranean-style diet was cross-sectionally associated with lower blood glucose and insulin levels, before adjustment for adiposity. Adjustment for waist circumference attenuated the association between the MeDiet and blood glucose; however, the relationship between the MeDiet and insulin levels remained statistically significant. The MeDiet was not related to the incidence of T2D.

Similar to the present findings, an inverse cross-sectional association was found between indices of glucose homeostasis and adherence to the MeDiet among non-diabetic subjects in Greece[21]. A recent study in French households comparing computer-simulated personalised diets with a 7 d food record of adults from French households in meeting dietary recommendations has also shown that foods typical of the MeDiet such as unrefined grains, legumes, nuts, fruits, fish and vegetables were efficient ways to achieve overall nutrient adequacy[9]. Additionally, current evidence indicates that adherence to a Mediterranean dietary pattern together with maintenance of ideal body weight appears to be an excellent strategy to reduce T2D risk[10,22].

Contrary to the present hypothesis, the Mediterranean dietary pattern was not related to a lower T2D incidence in this population. This is in contrast to previous published findings, such as the PREDIMED (Preverción con Dieta Mediterránea) study, a randomised trial in Spain, which indicated that consumption of the MeDiet led to a 50 % reduction in diabetes incidence over 4 years among non-diabetics at high CVD risk, and the observational Nurses' Health Study which found that after a 20-year follow-up, consumption of a Mediterranean-style diet was associated with a significantly lower risk of CVD, CHD and stroke[6,23]. A recent large prospective study (European Prospective Investigation Into Cancer and Nutrition Study: The InterAct project), which used nine dietary characteristic components of the MeDiet (score range 0–18), has also shown that adherence to the MeDiet was associated with a small reduction in the risk of developing T2D[24].

There are several limitations of the present study, which may explain the lack of association in the MESA population between the MedDiet score and incident diabetes. First, the MeDiet score might be inadequate for a multi-ethnic population in the USA, with dietary patterns very different from those traditionally observed in Mediterranean countries. As a second limitation, the present study attempted to define a Mediterranean dietary pattern from usual diets of participants using a dietary assessment tool not specifically designed to measure conformity to the MeDiet. Not all of the distinct food components of the traditional MeDiet were included in the questionnaire (e.g. olive oil). Furthermore, many of the components were part of line items, which included non-MeDiet foods in addition to the MeDiet food items. Our attempt to tease out specific food components from composite or mixed dishes might have possibly led to either overestimation or underestimation of some food categories. Third, measurement error associated with changes in the diet over the duration of follow-up could cause misclassification of the exposure. Unlike the Nurses' Health Study where there was updated dietary information, the MESA had only one dietary measure. This might be a possible explanation for the differences in the present findings[6]. Lastly, if the association between the MeDiet and incident diabetes is small in magnitude, we may have been underpowered to detect a relationship. Despite these limitations, the present study also has several important strengths, including the diverse population, use of objectively identified diabetes (not only self-report), and the highly standardised serum processing, anthropometric measurements and covariate assessment across the study centres.

Notably, a previous analysis of the MESA sample identified two empirically derived dietary patterns associated with the risk of diabetes[17]. In contrast to the previous work, our MeDiet index focused *a priori* on only those food groups that were commonly attributed to the Mediterranean cuisine. However, the percentage agreement of quintile ranks for the MeDiet score and each of the previous dietary patterns were about 35 %, indicating a fair to moderate agreement in how the dietary patterns were associated with the risk of T2D.

In the present study, we found that a high consumption of the MeDiet was associated with significantly lower serum insulin levels, but after adjustment for obesity was not related to glucose levels or the incidence of T2D. The new dietary guidelines for Americans, which are based on current epidemiological evidence, reiterate the need for a more plant-based diet, less processed meat, and more low-fat dairy products and seafood, which are typical components of the Mediterranean dietary pattern. The synergistic effect of these individual components of the MeDiet may give this dietary pattern its numerous beneficial properties in mitigating chronic diseases such as T2D. Overall, the present study supports the existing evidence that consistent consumption of a Mediterranean-type diet may lead to reduced risk for T2D. Given the beneficial properties of the traditional MeDiet, further research should determine whether this pattern

is applicable to and leads to similar health benefits in diverse ethnic groups with other culinary traditions.

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