## ORIGINAL ARTICLE

Epidemiology/Genetics

# Obesity O CHESITY WILEY

## A South Asian Mediterranean-style diet is associated with favorable adiposity measures and lower diabetes risk: The MASALA cohort

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#### Funding information

National Institutes of Health, Grant/Award Numbers: 2R01HL093009, 5R01HL093009, UL1RR024131, UL1TR001872

#### Abstract

**Objective:** The Mediterranean diet is associated with lower risks for type 2 diabetes (T2D) and cardiovascular disease in certain populations, although data among diverse groups are limited. This study evaluated cross-sectional and prospective associations between a novel South Asian Mediterranean-style (SAM) diet and cardiometabolic risk among US South Asian individuals.

**Methods:** The study included 891 participants at baseline in the Mediators of Atherosclerosis in South Asians Living in America (MASALA) study. Culturally relevant foods were grouped into nine categories to construct the SAM score. The study examined associations of this score with cardiometabolic risk factors and incident T2D.

**Results:** At baseline, higher adherence to the SAM diet was associated with lower glycated hemoglobin ( $-0.43\% \pm 0.15\%$  per 1-unit increase in SAM score; p = 0.004) and lower pericardial fat volume ( $-1.22 \pm 0.55$  cm<sup>3</sup>; p = 0.03), as well as a lower like-lihood of obesity (odds ratio [OR]: 0.88, 95% CI: 0.79–0.98) and fatty liver (OR: 0.82, 95% CI: 0.68–0.98). Over the follow-up ( $\sim$ 5 years), 45 participants developed T2D; each 1-unit increase in SAM score was associated with a 25% lower odds of incident T2D (OR: 0.75, 95% CI: 0.59–0.95).

**Conclusions:** A greater intake of a SAM diet is associated with favorable adiposity measures and a lower likelihood of incident T2D.

## INTRODUCTION

South Asian individuals represent one-quarter of the global population and include individuals with ancestry from Bangladesh, Bhutan, India, the Maldives, Nepal, Pakistan, and Sri Lanka. They are one of the most rapidly growing ethnic groups in the United States, with a population size of 5.4 million individuals as of 2017 [1]. Research has consistently shown that South Asian individuals have disproportionally increased risks of type 2 diabetes (T2D) and cardiovascular disease (CVD) compared with other populations, including White and other Asian American groups [2–5].

Various healthy dietary patterns are associated with lower risks of CVD and T2D in the broader population, and therefore they may be a compelling means to mitigate these consistently reported adverse health conditions among South Asian individuals. One such dietary pattern is the Mediterranean diet, a primarily plant-based dietary pattern that is characterized by higher intakes of vegetables, whole grains, olive oil, nuts, and beans and other legumes and lower intakes of animal proteins (with fish being the preferred source), as well as moderate alcohol intake. It has been associated with marked health benefits, including reduced risks of CVD [6], T2D [7], certain cancers [8], and overall mortality [9]. However, most studies investigating the health benefits of the Mediterranean diet have been conducted among those living in Mediterranean or European countries or among predominantly US-based White populations, whereas similar data among more diverse groups are limited [10].

Therefore, in the current study, we aimed to (1) adapt an existing Mediterranean diet score to be inclusive of foods consumed by the US South Asian population using data from a validated, ethnic-specific food frequency questionnaire (FFQ) and (2) examine the crosssectional and prospective associations of this score with a broad panel of cardiometabolic markers among those enrolled in the Mediators of Atherosclerosis in South Asians Living in America (MASALA) study.

## METHODS

#### Study population

The MASALA study is a community-based prospective cohort of South Asian men and women living in the San Francisco Bay area in California and the greater Chicago area in Illinois. A description of the MASALA study eligibility, methods, and measures has been published in detail previously [11]. Briefly, eligible cohort participants had South Asian ancestry, were ages 40 to 84 years at the time of enrollment, and were able to communicate in English, Hindi, or Urdu. Those with CVD at baseline were excluded. A total of 906 participants were enrolled and underwent the baseline clinical examination between October 2010 and March 2013. Participants returned for the second clinical examination between September 2015 and March 2018 (N = 749). In the current analysis, we excluded participants who reported implausible energy intakes (<800 kcal/d or >4000 kcal/d for men and <500 kcal/d or >3500 kcal/d for women), for a total of 891 and 735 participants at baseline and follow-up, respectively.

#### **Study Importance**

#### What is already known?

- South Asian individuals have a disproportionately high risk for cardiometabolic disease.
- The Mediterranean diet is associated with reduced risks for type 2 diabetes (T2D) and cardiovascular disease in certain populations, but data among diverse groups are scarce.

#### What does this study add?

- Our findings provide the first prospective evidence that a Mediterranean-style diet that incorporates traditional South Asian foods is associated with a lower risk of incident diabetes.
- This dietary pattern is also associated with favorable cross-sectional measures of body composition, glycated hemoglobin, and fatty liver.

# How might these results change the direction of research or the focus of clinical practice?

- Prior research has underscored the importance of studying and integrating culturally specific foods and dishes into dietary recommendations and lifestyle interventions to facilitate implementation among diverse communities.
- Accordingly, this Mediterranean-style dietary pattern that incorporates traditional South Asian foods may serve as a useful dietary strategy to prevent T2D in this high-risk population.

# Dietary assessment and Mediterranean-style diet score

Usual dietary intake over the previous year was assessed using the previously validated Study of Health Assessment and Risk in Ethnic Groups FFQ [12]. This ethnic-specific FFQ contains 163 food items (61 of which are unique to South Asian cuisine), and participants were asked to indicate their consumption frequency (per day, per week, per month, per year, or never) and serving size (either small or large relative to the specified average serving size) for each item.

Based on the previously developed Alternate Mediterranean Diet Score [13], we constructed a South Asian Mediterranean-style (SAM) diet score by grouping foods into nine predefined categories (vegetables, fruits, legumes, nuts, whole grains, red/processed meats, fish, alcohol, and monounsaturated to saturated fat ratio). Supporting Information Table S1 details what foods were included in each category. Participants consuming greater than the median intake received 1 point per category; those consuming between 5 g/d and 25 g/d of alcohol received 1 point; and red/processed meats were reversely scored. We summed these points for a possible SAM score ranging from 0 to 9, with higher scores reflecting greater adherence to the SAM diet.

## Ascertainment of cardiometabolic risk factors

At baseline, we collected measures of subclinical atherosclerosis, glycemia, dyslipidemia, blood pressure, uric acid, anthropometry, and computed tomography (CT) derived ectopic and subcutaneous fat depots. At the follow-up (approximately 5 years later), we collected updated measures of body weight, fasting glucose, glycated hemoglobin (HbA1c), and uric acid.

## Subclinical atherosclerosis

Participants underwent high-resolution B-mode ultrasonography (University of California, San Francisco: Vivid 7 ultrasound, GE Healthcare; Northwestern University: Acuson Sequoia C256, Siemens Healthcare) to measure right and left internal and common carotid artery intima-media thickness. The radiographic protocols for these measures have been described in detail previously [11, 14]. Cardiac CT scans were performed with gated-cardiac CT scanners (University of California, San Francisco: 16D scanner, Philips Medical Systems, or the MSD Aquilion 64 model, Toshiba Medical Systems; Northwestern University: Sensation Cardiac 64 scanner, Siemens Medical Solutions). Coronary calcification in each of the four major coronary arteries was quantified using the Agatston score, and the sum of the unadjusted score was used in our analysis [15].

## Glycemia measures

Fasting blood samples were collected by certified phlebotomists or nurses. At baseline and follow-up, fasting plasma glucose was measured using the hexokinase method (Ortho Clinical Diagnostics, Johnson & Johnson). HbA1c was measured using the immunoturbidimetry assay. Fasting serum insulin was measured using the sandwich immunoassay method (Roche Elecsys 2010, Roche Diagnostics).

At baseline, participants who were not taking diabetes medications underwent a 75-g oral glucose tolerance test. Blood samples of glucose and insulin were collected after 2 hours. The homeostatic model assessment for insulin resistance (a measure of insulin resistance) was calculated as (glucose [mmol/L] × insulin [ $\mu$ IU/mL]/22.5). β-cell function (a surrogate measure for insulin sensitivity) was estimated using the oral disposition index, which was calculated as ([ $\Delta$ insulin\_0-30/ $\Delta$ glucose\_0-30] × [1/fasting insulin]).

Participants were classified as having T2D if they were using a glucose-lowering medication and/or had fasting plasma glucose ≥7.0 mmoL/L and/or had 2-hour post-challenge glucose ≥11.1 mmol/L. Participants without T2D at baseline but who met the criteria at follow-up were defined as incident T2D cases.

## Dyslipidemia, inflammatory markers, and uric acid

Plasma concentrations of high-density lipoprotein (HDL), low-density lipoprotein (LDL), and triglycerides were measured at baseline and follow-up using enzymatic methods (Quest Diagnostics). Baseline high-sensitivity C-reactive protein was measured using the BN II nephelometer (Siemens Healthcare Diagnostics). Baseline serum total adiponectin was measured using Millipore Luminex adipokine panel A (EMD Millipore). Uric acid level was measured at baseline and follow-up using spectrophotometry (Quest Diagnostics). We defined hyperurice-mia as uric acid ≥7.0 mg/dL.

#### Body composition

Body weight, height, and waist circumference were measured by centrally trained study staff using a standard protocol [11]. Body mass index (BMI) was defined as the participant's weight in kilograms divided by height in meters squared. We defined overweight as BMI  $\geq$  23.0 and obesity as BMI  $\geq$  27.5 in accordance with the current World Health Organization recommendation for Asian populations [16], as has been done previously in this cohort [17]. Subcutaneous and visceral fat area was measured with abdominal CT using standard protocols [11]. Pericardial fat volume and hepatic fat attenuation were both obtained using noncontrast cardiac CT imaging. We defined fatty liver as <40 Hounsfield units [18].

#### Other cardiometabolic risk factors

Seated resting blood pressure was evaluated three times using an automated blood pressure monitor (V100 Vital Signs Monitor, GE Healthcare). An average of the final two readings was used for analysis. We defined hypertension as either the self-reported use of an antihypertensive medication or blood pressure  $\geq$  140/90 mm Hg.

### **Covariate assessment**

All participants provided information on personal history, demographics, socioeconomic status, medical history, medication use, and family history of relevant diseases at the baseline visit. Physical activity was measured as total metabolic equivalent minutes per week using the Typical Week's Physical Activity Survey, which was adapted from the Cross-Cultural Activity Participation Study [19]. Cultural beliefs and behaviors were assessed using a multidimensional measure of acculturation developed specifically for this cohort [20]. This seven-item traditional cultural beliefs scale is scored from 7 to 35, with higher values indicating weaker traditional South Asian beliefs, and it has previously shown good reliability and validity [20]. Routine experiences of interpersonal discrimination and unfair treatment were measured using the Everyday Discrimination Scale, a valid and reliable nine-item scale scored from 9 to 54, with higher values indicating more discrimination [21]. Total energy intake

TABLE 1 Baseline characteristics of participants enrolled in the MASALA cohort according to quartile of SAM score, 2010 to 2013

|  | SAM diet score           |                          |                          |                          |         |
|--|--------------------------|--------------------------|--------------------------|--------------------------|---------|
| n<br>Mean score                        | Quartile 1<br>153<br>1.7 | Quartile 2<br>355<br>3.5 | Quartile 3<br>172<br>5.0 | Quartile 4<br>211<br>6.5 | p value |
| Age (y)                                | 52.4 (0.8)               | 55.1 (0.5)               | 55.9 (0.7)               | 56.9 (0.7)               | <0.0001 |
| Female (%)                             | 45.8                     | 50.4                     | 44.2                     | 44.6                     | 0.38    |
| Duration lived in United States (y)    | 27.2 (0.8)               | 26.3 (0.5)               | 27.3 (0.7)               | 27.7 (0.7)               | 0.48    |
| Bachelor's degree or more (%)          | 83.7                     | 86.5                     | 90.1                     | 91.0                     | 0.02    |
| Family income of at least \$75,000 (%) | 78.0                     | 67.5                     | 73.2                     | 80.6                     | 0.11    |
| Sum of cultural tradition measures     | 14.4 (0.5)               | 13.6 (0.3)               | 13.6 (0.5)               | 14.8 (0.5)               | 0.67    |
| Everyday discrimination scale          | 16.1 (0.5)               | 15.0 (0.3)               | 14.8 (0.5)               | 14.5 (0.4)               | 0.03    |
| Dine out at least once per week (%)    | 46.4                     | 43.9                     | 44.2                     | 42.2                     | 0.47    |
| Current smokers (%)                    | 5.9                      | 3.1                      | 2.3                      | 1.9                      | 0.04    |
| Physical activity (MET-min/wk)         | 10,091 (347)             | 10,098 (213)             | 9751 (306)               | 10,585 (293)             | 0.47    |
| BMI (kg/m²)                            | 26.6 (0.3)               | 26.2 (0.2)               | 25.7 (0.3)               | 25.3 (0.3)               | 0.005   |
| Hyperlipidemia (%)                     | 81.1                     | 79.5                     | 82.7                     | 76.1                     | 0.36    |
| Hypertension (%)                       | 36.0                     | 41.7                     | 41.9                     | 38.4                     | 0.85    |
| Dietary factors                        |                          |                          |                          |                          |         |
| Energy (kcal/d)                        | 1278 (35)                | 1600 (23)                | 1781 (33)                | 2007 (30)                | <0.0001 |
| Carbohydrates (g/d)                    | 240.0 (2.2)              | 245.2 (1.3)              | 248.0 (1.9)              | 251.5 (1.8)              | <0.0001 |
| Protein (g/d)                          | 63.8 (0.8)               | 61.6 (0.5)               | 61.9 (0.7)               | 60.7 (0.7)               | 0.007   |
| Monounsaturated fat (g/d)              | 20.7 (0.4)               | 21.6 (0.2)               | 22.7 (0.4)               | 22.9 (0.3)               | <0.0001 |
| Polyunsaturated fat (g/d)              | 10.7 (0.2)               | 11.8 (0.1)               | 12.7 (0.2)               | 13.2 (0.2)               | <0.0001 |
| Saturated fat (g/d)                    | 18.0 (0.3)               | 15.6 (0.2)               | 13.8 (0.3)               | 12.4 (0.3)               | <0.0001 |
| Dietary fiber (g/d)                    | 16.8 (0.3)               | 19.7 (0.2)               | 22.1 (0.3)               | 23.9 (0.3)               | <0.0001 |
| Alcohol (g/d)                          | 2.5 (0.5)                | 3.2 (0.3)                | 1.8 (0.4)                | 2.6 (0.4)                | 0.58    |
| Food groups (servings/d)               |                          |                          |                          |                          |         |
| Fish and seafood                       | 0.16 (0.02)              | 0.12 (0.01)              | 0.12 (0.02)              | 0.13 (0.02)              | 0.34    |
| Red/processed meat                     | 0.27 (0.03)              | 0.19 (0.02)              | 0.10 (0.02)              | 0.04 (0.02)              | <0.0001 |
| Whole grains                           | 1.6 (0.1)                | 1.9 (0.1)                | 2.1 (0.1)                | 2.3 (0.1)                | <0.0001 |
| Legumes                                | 1.0 (0.1)                | 1.3 (0.0)                | 1.6 (0.1)                | 1.8 (0.1)                | <0.0001 |
| Fruits                                 | 2.0 (0.1)                | 2.4 (0.1)                | 2.8 (0.1)                | 3.3 (0.1)                | <0.0001 |
| Vegetables                             | 5.7 (0.2)                | 6.7 (0.1)                | 7.9 (0.2)                | 8.5 (0.2)                | <0.0001 |
| Nuts                                   | 0.37 (0.05)              | 0.65 (0.03)              | 1.01 (0.04)              | 1.24 (0.04)              | <0.0001 |
| Dairy products                         | 4.3 (0.2)                | 3.8 (0.1)                | 3.7 (0.1)                | 3.4 (0.1)                | <0.0001 |
| Sweets                                 | 0.74 (0.05)              | 0.63 (0.03)              | 0.46 (0.04)              | 0.48 (0.04)              | <0.0001 |

*Note*: Values are reported as either age, sex, and calorie adjusted mean (SE) or percentage using ANOVA for continuous variables and  $\chi^2$  tests for categorical variables.

Abbreviations: MASALA, Mediators of Atherosclerosis in South Asians Living in America; MET, metabolic equivalent; SAM, South Asian Mediterraneanstyle.

was assessed from the FFQ as kilocalories per day. All questionnaires were translated into Hindi and Urdu.

## **Statistical analysis**

We compared baseline characteristics of study participants across quartiles of SAM score using general linear regression adjusted for age, sex, and total energy intake for continuous variables and  $\chi^2$  tests for categorical variables. We tested for linear trends by assigning the median value to each quartile and treating this as a continuous variable in the regression model.

We evaluated the associations between SAM score and cardiometabolic risk factors using multivariable general linear regression for continuous outcomes and logistic regression for binary outcomes. We tested the assumptions of linear regression by examining the normal

**TABLE 2** Cross-sectional associations ( $\beta$  [SE]) between SAM diet score and measures of cardiometabolic risk among MASALA study participants at baseline

|  | Model 1: age, sex,<br>and energy adjustment | Model 2: multivariable adjustment <sup>a</sup> | Model 3: multivariable adjustment <sup>a</sup> + BMI |
|--|---|--|--|
| Subclinical measures of atherosclerosis    |   |  |  |
| Coronary artery calcium score <sup>c</sup> | -2.59 (4.57)                                | -2.78 (4.63)                                   | -2.17 (4.63)   |
| Common carotid IMT (mm) <sup>c</sup>       | -0.47 (0.48)                                | -0.43 (0.51)                                   | -0.29 (0.51)   |
| Internal carotid IMT (mm) <sup>c</sup>     | -0.56 (0.66)                                | -0.50 (0.68)                                   | -0.33 (0.68)   |
| Glycemia measures <sup>b</sup>             |   |  |  |
| Fasting glucose (mg/dL) <sup>c</sup>       | 0.01 (0.31)                                 | 0.13 (0.33)                                    | 0.16 (0.33)  |
| HbA1c (%) <sup>c</sup>                     | -0.43 (0.15) <sup>f</sup>                   | -0.45 (0.15) <sup>f</sup>                      | -0.43 (0.15) <sup>f</sup>                            |
| β-cell function <sup>c,d</sup>             | 0.00 (0.12)                                 | 0.01 (0.12)                                    | 0.01 (0.12)  |
| HOMA-IR <sup>c</sup>                       | -2.23 (1.70)                                | -1.05 (1.76)                                   | -0.84 (1.53)   |
| Plasma lipids                              |   |  |  |
| Triglycerides (mg/dL) <sup>c</sup>         | -0.54 (1.02)                                | 0.16 (1.07)                                    | 0.52 (1.05)  |
| HDL-C (mg/dL)                              | 0.06 (0.28)                                 | -0.14 (0.28)                                   | -0.23 (0.28)   |
| LDL-C (mg/dL)                              | -1.12 (0.72)                                | -0.51 (0.70)                                   | -0.42 (0.70)   |
| Inflammation and adipokines                |   |  |  |
| C-reactive protein $(\mu g/mL)^c$          | -6.09 (2.42) <sup>f</sup>                   | -3.95 (2.53)                                   | -2.46 (2.30)   |
| Adiponectin (mg/dL) <sup>c</sup>           | 0.76 (1.42)                                 | 0.80 (1.46)                                    | 0.53 (1.45)  |
| Other metabolic measures                   |   |  |  |
| Uric acid (mg/dL)                          | 0.00 (0.04)                                 | 0.04 (0.04)                                    | 0.06 (0.03)  |
| Body composition measures                  |   |  |  |
| BMI (kg/m²)                                | -0.24 (0.09) <sup>f</sup>                   | -0.16 (0.09)                                   | -  |
| Weight (kg)                                | -0.47 (0.26)                                | -0.22 (0.27)                                   | -  |
| Waist circumference (cm)                   | -0.49 (0.22) <sup>e</sup>                   | -0.29 (0.23)                                   | 0.02 (0.13)  |
| Subcutaneous fat area (cm <sup>2</sup> )   | -1.98 (2.22)                                | -1.05 (2.28)                                   | 1.39 (1.72)  |
| Visceral fat area (cm <sup>2</sup> )       | -3.07 (1.20) <sup>e</sup>                   | -2.83 (1.25) <sup>e</sup>                      | -1.35 (1.01)   |
| Pericardial fat volume (cm <sup>3</sup> )  | -2.37 (0.63) <sup>g</sup>                   | -1.81 (0.64) <sup>f</sup>                      | -1.22 (0.55) <sup>e</sup>                            |
| Hepatic fat attenuation (HU)               | 0.72 (0.23) <sup>f</sup>                    | 0.60 (0.24) <sup>e</sup>                       | 0.45 (0.22) <sup>e</sup>                             |

*Note*: All values are presented as  $\beta$  (SE) per 1-unit increase in SAM score.

Abbreviations: HbA1c, glycated hemoglobin; HDL-C, high-density lipoprotein cholesterol; HOMA-IR, homeostatic model assessment for insulin resistance; HU, Hounsfield unit; IMT, intima-media thickness; LDL-C, low-density lipoprotein cholesterol; MASALA, Mediators of Atherosclerosis in South Asians Living in America; SAM, South Asian Mediterranean-style.

<sup>a</sup>Adjusted for age, sex, total energy intake, years lived in the United States, education level, family income, physical activity, perception of discrimination, the traditional cultural beliefs scale, tobacco pack years of smoking, family history of diabetes, use of diabetes medication (except for glycemia measures), cholesterol-lowering medication, and hypertension medication.

<sup>b</sup>Participants with diabetes were excluded from these four measures.

<sup>c</sup>Values were log-transformed to obtain a normal distribution of the residuals. For outcomes that were log-transformed, values represent percentage increase in outcome variable for every 1-unit increase in SAM score.

<sup>d</sup>Measured using the oral disposition index.

<sup>e</sup>p < 0.05.

<sup>f</sup>p < 0.01.

 $^{g}p < 0.001.$ 

probability plots of the residuals and the residual versus predicted plots. Where necessary, we log-transformed the outcome variables and reexamined each diagnostic plot.

In the first multivariable model, we adjusted for age, sex, and total energy intake (model 1). We further adjusted for education level, family income, number of years lived in the United States, physical activity, perception of discrimination, the traditional cultural beliefs scale, tobacco pack years of smoking, family history of diabetes (parents and siblings), use of diabetes medication, cholesterol-lowering medication, and hypertension medication in model 2. Based on prior literature, we hypothesized a priori that measures of discrimination and cultural beliefs could confound our associations of interest [20, 22–24]. Finally, because these associations could potentially be mediated by BMI, we adjusted for it separately in model 3. For all linear models, results are presented as the unit change (or percentage change for log-transformed variables) in outcome per 1-unit increase in SAM

score. To minimize potential confounding by prevalent disease, we excluded participants with T2D in analyses in which glycemia measures were the outcome. For all prospective associations, we adjusted for the baseline value of the covariates and of the corresponding outcome measure. Finally, for the association between SAM score and incident T2D, we tested for potential effect modification by age, sex, diabetes family history, obesity status, and physical activity level by including cross-product terms between these variables and the SAM score variable. All statistical tests were two-sided and were conducted using SAS version 9.4 (SAS Institute Inc.).

### **Ethics**

The MASALA study protocol was approved by the Institutional Review Boards of the University of California, San Francisco and Northwestern University, Chicago. The current analysis protocol was approved by the Institutional Review Board of Brigham and Women's Hospital, Boston, Massachusetts. All participants provided written informed consent.

## RESULTS

#### **Baseline characteristics**

Participant characteristics at baseline are shown in Table 1. Compared with participants in the lowest quintile of SAM score, those in the uppermost quintile were older (56.9 vs. 52.4 years in Q4 and Q1, respectively; *p* for trend < 0.0001), more often held a bachelor's degree (91.0% vs. 83.7%; *p* for trend = 0.02), reported fewer experiences of discrimination (score of 14.5 vs. 16.1; *p* for trend = 0.03), were less likely to be smokers (1.9% vs. 5.9%; *p* for trend = 0.04), and had a lower BMI (25.3 vs. 26.6 kg/m<sup>2</sup>; *p* for trend = 0.005). Those in the highest quintile of SAM score also reported greater intakes of carbohydrates, dietary fiber, and total energy but lower intakes of protein and saturated fat.

#### **Cross-sectional analysis**

All cross-sectional associations between SAM score and measures of cardiometabolic risk at baseline are shown in Table 2. At baseline, each 1-unit increase in SAM score was associated with lower HbA1c in the fully adjusted model ( $-0.43\% \pm 0.15\%$ ; p = 0.004). No other measures of glycemia were significantly associated with SAM score at baseline. A higher SAM score was significantly and inversely associated with lower high-sensitivity C-reactive protein concentration after adjusting for age, sex, and total energy intake, but this association was attenuated after multivariable adjustment.

For body composition measures, each 1-unit higher SAM score was associated with lower BMI ( $-0.24 \pm 0.09 \text{ kg/m}^2$ ; p = 0.008) after adjusting for age, sex, and energy intake, although this association was

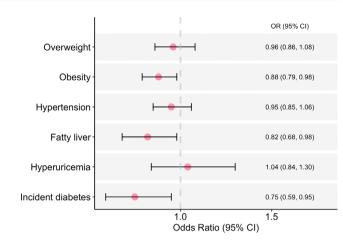


FIGURE 1 Likelihood (OR [95% CI]) of cardiometabolic risk and incident type 2 diabetes per 1-unit increase in South Asian Mediterranean-style diet score among MASALA study participants. Fatty liver is defined as liver-spleen attenuation < 40 Hounsfield units. Hypertension is defined using the National Cholesterol Education Program criteria as blood pressure ≥ 140/90 mm Hg or use of medication. Obesity is defined as BMI  $\geq$  27.5 kg/m<sup>2</sup>. Overweight is defined as BMI ≥ 23. Hyperuricemia is defined as serum uric acid  $\geq$  7 mg/dL. All models were adjusted for age, sex, total energy intake, years lived in the United States, education level, family income, physical activity, perception of discrimination, the traditional cultural beliefs scale, tobacco pack years of smoking, family history of diabetes, use of diabetes medication (except for incident diabetes outcome), cholesterol-lowering medication, hypertension medication (except for hypertension outcome), and BMI (except for overweight and obesity outcomes). OR, odds ratio; MASALA, Mediators of Atherosclerosis in South Asians Living in America [Color figure can be viewed at wileyonlinelibrary.com]

attenuated after multivariable adjustment. When we examined the likelihood of overweight and obesity, after multivariable adjustment, each 1-unit increase in SAM score was associated with 12% lower odds of obesity (odds ratio [OR]: 0.88, 95% confidence interval [CI]: 0.79-0.98) but not overweight (OR: 0.96, 95% CI: 0.86-1.08; Figure 1). A higher SAM score was not significantly associated with subcutaneous fat area but was initially associated with lower visceral fat area (-2.83  $\pm$  1.25 cm<sup>2</sup>; p = 0.02). However, this did not remain significant after further adjustment for BMI. Finally, in our fully adjusted models, each 1-unit increase in SAM score was significantly associated with lower pericardial fat volume ( $-1.22 \pm 0.55$  cm<sup>3</sup>; p = 0.03), higher hepatic fat attenuation (0.45  $\pm$  0.22 Hounsfield units; p = 0.045), and lower odds of fatty liver disease (OR: 0.82, 95% CI: 0.68-0.98; Figure 1). We found no evidence of an association between SAM score and measures of subclinical atherosclerosis, blood lipids, adiponectin, hyperuricemia, or hypertension in any of the models.

#### **Prospective analysis**

In prospective analyses ( $\sim$ 5 years after baseline), we identified 45 cases of incident diabetes. After multivariable adjustment, for each 1-unit higher SAM score the odds of incident T2D were 25% lower

**TABLE 3** Prospective associations ( $\beta$  [SE]) between SAM diet score and measures of cardiometabolic risk among MASALA study participants at the follow-up visit

|                                      | Model 1: age, sex,<br>and energy adjustment | Model 2: multivariable adjustment <sup>a</sup> | Model 3: multivariable adjustment <sup>a</sup> + BMI |
|--------------------------------------|---|--|--|
| Glycemia measures <sup>b</sup>       |   |  |  |
| Fasting glucose (mg/dL) <sup>c</sup> | -0.18 (0.29)                                | -0.21 (0.30)                                   | -0.19 (0.30)   |
| HbA1c (%) <sup>c</sup>               | 0.14 (0.15)                                 | 0.05 (0.16)                                    | 0.05 (0.16)  |
| Plasma lipids                        |   |  |  |
| Triglycerides (mg/dL) <sup>c</sup>   | -0.10 (0.87)                                | -0.51 (0.90)                                   | -0.39 (0.90)   |
| HDL-C (mg/dL)                        | -0.04 (0.21)                                | -0.06 (0.21)                                   | -0.06 (0.21)   |
| LDL-C (mg/dL)                        | -0.86 (0.72)                                | -0.72 (0.74)                                   | -0.78 (0.74)   |
| Other metabolic measures             |   |  |  |
| Uric acid (mg/dL)                    | 0.02 (0.03)                                 | 0.02 (0.03)                                    | 0.03 (0.03)  |
| Body composition measures            |   |  |  |
| BMI (kg/m <sup>2</sup> )             | -0.02 (0.04)                                | -0.01 (0.05)                                   | -  |
| Weight (kg)                          | -0.12 (0.10)                                | -0.12 (0.11)                                   | -  |
| Waist circumference (cm)             | -0.29 (0.17)                                | -0.26 (0.16)                                   | -0.20 (0.15)   |

Note: All values are presented as  $\beta$  (SE) per 1-unit increase in SAM score. All p values > 0.05.

Abbreviations: HbA1c, glycated hemoglobin; HDL-C, high-density lipoprotein; LDL-C, low-density lipoprotein; MASALA, Mediators of Atherosclerosis in South Asians Living in America; SAM, South Asian Mediterranean-style.

<sup>a</sup>Adjusted for age, sex, total energy intake, years lived in the United States, education level, family income, physical activity, perception of discrimination, the traditional cultural beliefs scale, tobacco pack years of smoking, family history of diabetes, use of diabetes medication (except for glycemia measures), cholesterol-lowering medication, hypertension medication, and baseline value of the corresponding cardiometabolic risk marker. <sup>b</sup>Participants with diabetes were excluded from these two measures.

<sup>c</sup>Values were log-transformed to obtain a normal distribution of the residuals. For outcomes that were log-transformed, values represent percentage increase in outcome variable for every 1-unit increase in SAM score.

(OR: 0.75, 95% CI: 0.59–0.95; Figure 1). We found no evidence of effect modification of this association according to age, sex, family history of diabetes, obesity status, or physical activity (all p for interaction > 0.05). Finally, we found no evidence of an association between baseline diet scores and follow-up measures of fasting glucose, HbA1c, triglycerides, HDL cholesterol, and LDL cholesterol or measures of anthropometry (Table 3).

## DISCUSSION

In this community-based prospective cohort study of South Asians, we found that a greater intake of a Mediterranean-style diet inclusive of foods commonly consumed by this population was associated with more favorable baseline measures of body composition (including pericardial fat volume and fatty liver) and HbA1c. Moreover, we found that this dietary pattern was associated with a lower risk of incident T2D after approximately 5 years of follow-up. These associations were independent of known confounders such as age, sex, years lived in the United States, measures of socioeconomic status, lifestyle factors, comorbidities, medication use, and BMI. These data suggest that a Mediterranean-style diet may be a useful dietary strategy to help prevent T2D in this high-risk population.

The inverse associations between a higher SAM score and measures of ectopic fat observed in our study deserve comment. Ectopic fat is a major independent risk factor for cardiometabolic disease including T2D [25–29]. Compared with other ethnic groups, South Asians tend to have a less favorable body composition profile that is characterized by greater levels of ectopic fat depots, including intermuscular and hepatic fat [30], which may partly explain the disparities in CVD and T2D risk among this population [31–34]. Given the rising cardiometabolic public health concerns, adherence to a healthy dietary pattern such as a Mediterranean-style diet is a readily implementable strategy to mitigate these disparities. Further experimental studies are warranted to confirm these observational findings.

The Mediterranean diet has been previously shown to be associated with health benefits, including lower risks of T2D and CVD [6, 7], although data among South Asians are very limited. Nevertheless, our findings are consistent with previous studies that examined the association between a Mediterranean-style diet (or components of this diet) and cardiometabolic risk among members of this population. An India-based randomized trial evaluated the potential cardioprotective effect of an Indo-Mediterranean diet (which encouraged high intakes of fruits, vegetables, nuts, whole grains, legumes, and mustard seed or soybean oil) among individuals considered to be at high risk for coronary artery disease [35]. Participants consuming the Indo-Mediterranean diet had significant decreases in LDL cholesterol, triglycerides, fasting blood glucose, blood pressure, and BMI, as well as fewer nonfatal myocardial infarctions and sudden cardiac deaths [35]. Nigam and colleagues conducted a randomized trial among Asian Indian men with nonalcoholic fatty liver disease to examine the effect of consuming olive or canola oil (both high in monounsaturated fatty acids, the cornerstone and main source of fat in the Mediterranean diet) and reported improvements in BMI, insulin resistance, blood lipids, and fatty liver grading after 6 months [36]. To our knowledge, our study is the first to document an inverse association between a Mediterranean-style diet and selected cardiometabolic factors among a broader cohort of South Asian immigrants in the United States and the first to document an inverse association between this dietary pattern and incident T2D among South Asian individuals.

Prior research suggests that a Mediterranean-style diet is enjoyable and sustainable in the long term. For example, participants in the Dietary Intervention Randomized Controlled Trial (DIRECT) who were randomized to consume a Mediterranean diet lost  $\sim$ 50% more weight at the end of the 2-year follow-up than those consuming a low-fat diet [37]. When these participants were followed for an additional 4 years, those in the Mediterranean diet group regained the least amount of weight lost in the original trial (1.4 kg vs. 2.7 and 4.1 kg in the low-fat and lowcarbohydrate groups, respectively; p = 0.004 for all comparisons) [38]. A post-experimental qualitative study of middle-aged UK adults found that participants considered the Mediterranean diet to be "enjoyable" and a "better guality of food" [39]. However, these individuals also felt that it was initially challenging to adapt to this eating pattern and that it resulted in greater food costs [39]. Similar studies would be useful to help inform potential barriers and to further guide implementation among South Asian individuals in the United States.

A 2019 consensus report highlighted the importance of integrating cultural factors and preferences to individualize nutrition therapy for adults with diabetes or prediabetes [40]. To date, the majority of research on the Mediterranean diet has been conducted among predominantly White populations living in Europe or the United States without taking into account food items and dishes that may be consumed by different ethnic groups [10]. To our knowledge, our study is the first to develop a comprehensive Mediterranean-style diet score that incorporates culturally relevant foods consumed by South Asian individuals, which may facilitate the uptake of this healthful dietary pattern among this population. Indeed, prior research found that a sample of British Pakistani and Indian individuals reduced the overall amount of South Asian foods they consumed after receiving a T2D diagnosis [41]. Many of these participants were advised by health care providers to stop eating their traditional diets, which drove their belief that these foods were collectively "damaging" [41]. Similarly, participants in a UK qualitative study conducted among ethnically diverse older adults also described receiving negative educational messages about their traditional foods [42]. Participants noted that they were often advised to stop consuming these foods altogether, which was viewed as unrealistic, as food is tied to cultural identity [42]. A Canadian qualitative study among African Nova Scotians and Punjabi British Columbians also described a close relationship between eating patterns and identity, and these participants reported that they were unlikely to avoid eating the foods that they were used to [43]. Taken together, these data underscore the importance of studying and integrating culturally specific foods and dishes into dietarv

recommendations and lifestyle interventions. Indeed, a communitybased and culturally salient lifestyle intervention among South Asian individuals was found to be effective and to maintain full participant retention, and continued research in this area is warranted [44].

The 2020-2025 Dietary Guidelines for Americans described three dietary patterns (healthy US-style eating pattern, vegetarian pattern, and Mediterranean-style pattern) that offer greater flexibility in food choices across a set of shared core elements (vegetables, fruits, grains, low-fat dairy, protein foods, and oils) [45]. Accordingly, our findings add to the growing literature of dietary patterns that are associated with a favorable metabolic risk profile among South Asians. An earlier study conducted among MASALA cohort participants found that a dietary pattern rich in fruits, vegetables, nuts, and legumes (a "prudent" pattern) was associated with lower odds of hypertension and metabolic syndrome as well as lower insulin resistance [46]. A vegetarian diet pattern was associated with lower BMI, fasting glucose, and insulin resistance, as well as lower odds of fatty liver [47]. Those in the vegetarian group did not consume seafood or alcohol [47], which differentiates the diet from the SAM score constructed in the current study (which positively scored both seafood and moderate alcohol intake). Finally, a plant-based eating pattern that specifically emphasized greater intakes of healthy plant foods was found to be associated with lower odds of both T2D and fatty liver [48]. These findings are consistent with our study of a Mediterranean-style diet that also emphasizes healthy plant foods. Taken together, these studies among a US South Asian population provide several options for tailored risk reduction to suit comorbidity profiles among this population.

The strengths of our study deserve comment. First, we used a validated ethnic-specific FFQ to previously construct а Mediterranean-style diet score that is inclusive of foods commonly consumed among the South Asian community. This allowed us to better capture the usual diet of study participants and also has practical implications for supporting the adoption of this dietary pattern in the community. Next, the MASALA study is, to our knowledge, the only prospective cohort of US South Asian individuals with detailed data on cardiometabolic risk factors (including subclinical atherosclerosis and body composition obtained using imaging methods) and other potential confounders such as a measure of cultural traditions and experiences of discrimination, which allowed us to adjust for a comprehensive list of confounders. However, our study is not without its limitations. As in any observational study, residual confounding is a possibility, although we adjusted for a large number of known and potential confounders. We did not collect data on food preparation methods for all items on the FFQ, which may lead to some misclassification of diet. Furthermore, the FFQ did not collect detailed data on specific oil intake, which is of interest to a Mediterranean-style diet; however, both monounsaturated fatty acid and polyunsaturated fatty acid intake tended to increase with increasing SAM score. Next, we did not have data on all cardiometabolic risk factors at the follow-up visit. Moreover, we used a baseline assessment of diet in our prospective analysis; therefore, future studies of longer-term habitual intake in this population would be valuable. Finally, our findings can be

extrapolated most directly to Asian Indian adults who are living in the United States because MASALA included only small proportions of immigrants from Pakistan, Bangladesh, and other countries.

In conclusion, our findings provide the first prospective evidence that a SAM diet is associated with a lower risk of incident diabetes, as well as favorable cross-sectional measures of body composition, HbA1c, and fatty liver. This dietary pattern may serve as a useful dietary strategy to prevent T2D in this high-risk population.O

### AUTHOR CONTRIBUTIONS

Sharan K. Rai and Shilpa N. Bhupathiraju designed the study. Sharan K. Rai conducted the statistical analysis. Sharan K. Rai and Shilpa N. Bhupathiraju interpreted the study results, drafted or revised the manuscript, and approved the final version of the manuscript. Steven L. Gortmaker contributed to study design, interpretation of study results, and revision of the manuscript and approved the final version of the final version of the manuscript. Frank B. Hu, Alka M. Kanaya, Namratha R. Kandula, and Qi Sun contributed to interpretation of study results and revision of the manuscript and approved the final version of the manuscript. All authors have approved the final version to be published. All authors agree to be accountable for all aspects of the work.

#### ACKNOWLEDGMENTS

The authors thank the other investigators, the staff, and the participants of the MASALA study for their valuable contributions.

The results of the current study were presented as a poster at the American Heart Association (AHA) EPI Lifestyle Scientific Sessions, May 20–21, 2021, held virtually because of the COVID-19 pandemic.

#### FUNDING INFORMATION

The project described was supported by National Institutes of Health (NIH) grants 5R01HL093009 and 2R01HL093009 and at the University of California, San Francisco site with grants UL1RR024131 and UL1TR001872. Sharan K. Rai was supported by a Doctoral Foreign Study Award from the Canadian Institutes of Health Research. The funding agencies had no role in the design and conduct of the study; collection, management, analysis, or interpretation of the data; preparation, review, or approval of the manuscript; or decision to submit the manuscript for publication.

#### CONFLICT OF INTEREST STATEMENT

Shilpa N. Bhupathiraju is a scientific consultant to LayerIV for work outside the submitted work. The other authors declared no conflict of interest.

#### DATA AVAILABILITY STATEMENT

Data described in the article, code book, and analytic code will not be made publicly available. Further information including the procedures to obtain and access data from the MASALA study is described at https://www.masalastudy.org/for-researchers

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## SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Rai SK, Gortmaker SL, Hu FB, et al. A South Asian Mediterranean-style diet is associated with favorable adiposity measures and lower diabetes risk: The MASALA cohort. *Obesity (Silver Spring)*. 2023;31(6): 1697-1706. doi:10.1002/oby.23759