

Mediators of Atherosclerosis in South Asians Living in America (MASALA) Study: Objectives, Methods, and Cohort Description

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ABSTRACT

Background: South Asians (individuals from India, Pakistan, Bangladesh, Nepal, and Sri Lanka) have high rates of cardiovascular disease (CVD) that cannot be explained by traditional risk factors. There are few prospective cohort studies investigating antecedents of CVD in South Asians.

Objectives: The Mediators of Atherosclerosis in South Asians Living in America (MASALA) study is investigating the prevalence, correlates, and outcomes associated with subclinical CVD in a population-based sample of South Asian men and women age 40–79 years at 2 US clinical field centers.

Population and Methodology: This cohort is similar in methods and measures to the Multi-Ethnic Study of Atherosclerosis (MESA) to allow for efficient cross-ethnic comparisons. Measurements obtained at the baseline examination include sociodemographic information, lifestyle and psychosocial factors, standard CVD risk factors, oral glucose tolerance testing, electrocardiography, assessment of microalbuminuria, ankle and brachial blood pressures, carotid intima-media wall thickness using ultrasonography, coronary artery calcium measurement, and abdominal visceral fat measurement using computed tomography. Blood samples will be assayed for biochemical risk factors. Between October 2010 and March 2013, we enrolled 906 South Asians with mean age of 55 ± 9 years (46% women; 98% immigrants who have lived 27 ± 11 years in the United States). The sociodemographic characteristics of this cohort are representative of US South Asians. Participants are being followed with annual telephone calls for identification of CVD events including acute myocardial infarction and other coronary heart disease, stroke, peripheral vascular disease, congestive heart failure, therapeutic interventions for CVD, and mortality.

Conclusions: The MASALA study will provide novel data on the prevalence and associations of cardiovascular risk factors and subclinical atherosclerosis in South Asians living in the United States.

Introduction

South Asians (individuals from India, Pakistan, Nepal, Bangladesh, and Sri Lanka) represent a quarter of the world's population and are the second fastest growing

ethnic group in the United States, with approximately 3.4 million US residents.¹ Several cross-sectional studies conducted worldwide have reported a high prevalence of diabetes mellitus (DM), hypertension, and cardiovascular

The MASALA study centers and investigators. Field Centers: University of California, San Francisco (Principal Investigator Alka Kanaya; Peter Ganz). Northwestern University (Principal Investigator Namratha Kandula; Kiang Liu, James Carr). Ultrasound Reading Center: Wake Forest University Medical Center (Principal Investigator David Herrington; Charles Tegeler, Greg Evans, Julia Fleshman). CT Reading Center: Harbor-UCLA Research and Education Institute (Principal Investigator Matthew J. Budoff; Chris Dailing). Coordinating Center: University of California, San Francisco (Principal Investigator Alka Kanaya; Stephen Hulley, Ann Chang, Eric Vittinghoff, Michael Schembri).

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disease (CVD) in this ethnic group, despite low body mass index. However, there are few longitudinal studies of South Asians to determine causes for this increased cardiometabolic risk and other factors that may explain the high prevalence of CVD.

Studies of native and migrant South Asians^{2–7} have shown a high prevalence of CVD. However, the majority of data on CVD in South Asians is derived from cross-sectional studies or death statistics.^{8,9} Studies from the United Kingdom and Singapore with mortality follow-up reported significantly higher rates of incident coronary heart disease (CHD) in South Asian men compared with other ethnic groups.^{10,11} There are no studies that have investigated the natural history of atherosclerosis and CVD outcomes in South Asians.

The Mediators of Atherosclerosis in South Asians Living in America (MASALA) study aims to create a longitudinal cohort of South Asians to examine the etiology and prognostic significance of subclinical atherosclerosis. This project utilizes the methods and measures of a large ongoing Multi-Ethnic Study of Atherosclerosis (MESA)^{12,13} to efficiently and innovatively compare disease prevalence and risk-factor associations among South Asians and 4 other ethnic groups in the United States. The objectives of the MASALA study are (1) to determine traditional, sociocultural, behavioral, and novel risk factors associated with subclinical atherosclerosis in US residents with South Asian origin; and (2) to compare the adjusted prevalence of subclinical atherosclerosis and cardiovascular risk factors to the 4 ethnic groups in MESA. An exploratory objective is to assess the prognostic significance of subclinical atherosclerosis by examining incident CVD events during the study period. Here we describe the study methods and demographic characteristics of the MASALA study cohort.

Methods

Study Design and Setting

We are conducting a prospective cohort study of a community-based sample of 900 South Asian men and women from 2 clinical sites: the San Francisco Bay Area at the University of California, San Francisco (UCSF), and the greater Chicago area at Northwestern University (NWU). The first study examination began in October 2010 and final participant enrollment concluded in March 2013. All participants were screened for study eligibility by telephone and were invited to the clinical site for a 6-hour baseline clinical examination at these clinical field centers. Annual telephone follow-up calls will be conducted to ascertain interim cardiovascular events or hospitalizations. Study enrollment was stratified by sex and age at each clinical site, with approximately equal enrollment by sex for each age decade (age 40–49 years, 50–59 years, 60–69 years, and 70–79 years). The UCSF and NWU institutional review boards approved the protocol.

Eligibility Criteria

To be eligible for the MASALA study, participants had to have (1) South Asian ancestry, defined by having ≥ 3 grandparents born in one of the following countries: India,

Pakistan, Bangladesh, Nepal, or Sri Lanka; (2) age between 40 and 79 years; and (3) ability to speak and/or read English, Hindi, or Urdu. A pilot study called the Metabolic Syndrome and Atherosclerosis in South Asians Living in America (National Institutes of Health grant no. K23 HL080026) had similar eligibility criteria and methods as this larger study. The 150 participants enrolled in the pilot study were eligible to enroll in the current MASALA study.

We used exclusion criteria identical to MESA,¹² which included having a physician-diagnosed myocardial infarction (MI), stroke, or transient ischemic attack; heart failure, angina, use of nitroglycerin; or those with a history of cardiovascular procedures such as coronary artery bypass graft surgery, angioplasty, valve replacement, pacemaker or defibrillator implantation, or any surgery on the heart or arteries. Those with current atrial fibrillation or undergoing active treatment for cancer were excluded. Those with life expectancy < 5 years due to a serious medical illness, impaired cognitive ability as judged by the reviewer, plans to move out of the study region in the next 5 years, or those living in a nursing home or on a waiting list for one were also excluded. Due to computed tomography (CT) scanner limitations, those weighing > 136 kg (300 lb) were excluded.

Recruitment

We employed telephone-based recruitment methods, similar to the MESA study,¹² and did not use a formal multistage probability sampling to be consistent with MESA. The sampling frames were created by clinical site and included all 9 counties of the San Francisco Bay Area for the UCSF field site, and the 7 census tracts closest to the NWU medical center and secondary suburban locations around Chicago where census data revealed high proportions of South Asian residents. Name, address, and telephone number were obtained for approximately 10 000 households in the targeted census tracts from commercial mailing list companies (InfoUSA, Omaha, NE; and Marketing Systems Group, Horsham, PA). Random samples of South Asian surnames from the desired geographic locations were created using specific algorithms. InfoUSA uses a cultural coding algorithm to identify 162 ethnicities, 16 ethnic groups, 80 language preferences, 21 countries of origin, and 12 religions using a 5-step matching process to classify a person's first and last name.

Prior to recruitment, the purpose, rationale, and design of the study were publicized to the residents of the target areas by seeking endorsements from community leaders; by giving presentations to community centers, religious centers, and social service and other specific organizations; and by soliciting publicity from local newspapers.

Every 2 to 4 weeks, a random batch of 100 letters was mailed with an invitational letter about the study and a brochure explaining the study rationale and measures. Each letter had a unique household identification number so that individual responses were tracked by our computerized tracking system. Two weeks after sending out the letter, telephone calls were conducted to enumerate the number of eligible and interested candidates in the household. After a short interview to determine eligibility and willingness

to participate, individuals were invited to participate in the study. If >1 person was eligible in the household, only 1 would be selected. A second letter was sent if there was no response within 1 to 2 months. All study recruiters were bilingual in English and Hindi or Urdu to facilitate communication with limited-English-proficiency participants.

Clinical Examination Components

After a requested 12-hour fast, written informed consent was obtained from participants upon their arrival to the clinical field center. All visits were conducted by trained bilingual study staff and all consent forms and questionnaires were also translated into Hindi and Urdu. Table 1 provides a list of examination components for the baseline study visit.

Twelve-lead electrocardiography (ECG) recordings were obtained using a Marquette MAC-1200 portable ECG instrument (General Electric/Marquette Electronics, Milwaukee, WI). The protocol for obtaining resting ECG was identical to that of the MESA baseline exam. Those with atrial fibrillation on ECG were excluded from study participation.

Questionnaire Measures

We gathered information on participants' contacts, demographic data, language use, tobacco use, alcohol consumption, medical conditions, access to medical care, family history of CVD and DM, reproductive history (women only), and current prescription and nonprescription medication and supplement use, including ayurvedic and other herbal medications. Physical activity was assessed using the Typical Week's Physical Activity Questionnaire.¹⁴ Dietary intake over the previous year was assessed using the Study of Health Assessment and Risk in Ethnic Groups (SHARE) food frequency questionnaire, which was created and validated among South Asians in Canada.¹⁵ Several psychosocial scales were administered similar to the MESA baseline clinical examination: the Spielberger trait anger and anxiety scales,¹⁶ the Center for Epidemiologic Studies depression scale,¹⁷ and those for social support,¹⁸ chronic psychological stress,¹⁹ perception of discrimination,^{20,21} and neighborhood environment.²²

Physical Exam Components

Seated resting blood pressure was measured 3 times using an automated blood pressure monitor (V100 Vital Signs Monitor; GE Healthcare, Fairfield, CT) with the average of the last 2 readings being used for analysis. Participant weight was measured on a standard balance-beam scale or digital weighing scale, and height was measured using a stadiometer. Waist circumference was measured using a flexible tape measure at the site of maximum circumference midway between the lower ribs and the anterior superior iliac spine. Hip circumference was measured at the maximum circumference of the buttocks.

Ankle-brachial blood pressure index was measured using a Doppler apparatus (EN50 LE 100; Nicolet Vascular,

Table 1. Components of the Baseline MASALA Study Examination, 2010–2013

Component	Scales Administered
Personal history, demographic data, socioeconomic status	Same as MESA baseline questionnaire, additional South Asian questions
Medical history	Same as MESA baseline questionnaire
Family history	Same as MESA baseline questionnaire
Medications, vitamins/supplements inventory	Same as MESA baseline questionnaire
Psychosocial assessment	Same as MESA baseline questionnaire
Dietary intake assessment	SHARE food-frequency questionnaire ¹⁵
Physical activity	Same as MESA baseline questionnaire ¹⁴
Sleep apnea assessment	Berlin sleep questionnaire ³⁰
Neighborhood assessment	Same as MESA baseline questionnaire
Cultural beliefs and behaviors	
Anthropometry	
Seated BP	
12-lead ECG	
Spot urine collection for microalbuminuria	
Phlebotomy (fasting)	
2-hour glucose tolerance; 30- and 120-minute phlebotomy	Not done for participants taking DM medications
ABI	
Carotid ultrasound	
Cardiac CT scan	
Abdominal CT scan	
Abbreviations: ABI, ankle-brachial index; BP, blood pressure; CT, computed tomography; DM, diabetes mellitus; ECG, electrocardiogram; MASALA, Mediators of Atherosclerosis in South Asians Living in America; MESA, Multi-Ethnic Study of Atherosclerosis; SHARE, Study of Health Assessment and Risk in Ethnic groups	

Golden, CO). The participant lay supine and systolic blood pressure measurements were taken from the brachial artery, the dorsalis pedis artery, and the posterior tibial artery of both the left and right side, using the protocol identical to MESA.

Phlebotomy was conducted by certified phlebotomists or nurses to obtain approximately 100 mL of blood while the participant was in a fasting state. Aliquots were processed for central analysis and storage at UCSF (approximately 40 aliquots per participant). Measurements planned include lipids and lipoproteins, inflammatory markers, insulin resistance, and other CVD biomarkers. Whole-blood samples were obtained and saved (approximately 7 mL) for

future DNA extraction, and PAXgene tubes were collected for future mRNA analysis. A random urine sample was collected for measurement of microalbuminuria and the remainder was stored for future studies.

Participants who were not taking DM medications underwent an oral glucose tolerance test. A 75-g oral glucose load was administered with blood samples taken from a peripheral vein at time 0, 30, and 120 minutes for the measurement of plasma glucose and insulin concentrations. The total amount of blood taken for this procedure was approximately 15 mL. We will measure surrogate measures of insulin resistance including fasting insulin, 2-hour insulin, and the homeostasis model assessment²³ and β -cell function.²⁴

Radiographic Measures

High-resolution B-mode ultrasonography was conducted for measurement of right and left internal and common carotid artery intima-media thickness (cIMT). To perform carotid ultrasound recordings, at UCSF the GE Vivid 7 ultrasound system with an 8-MHz linear array transducer (General Electric Healthcare) was used, and at NWU the Acuson Sequoia C256 system (Siemens Healthcare, Mountain View, CA) was used. The vascular technician located the bifurcation of the carotid artery, distinguished the internal from external carotid artery, and identified the maximal wall thickening in the near or far wall, in the carotid bulb or internal carotid artery. The cIMT was measured in 12 predefined segments (6 per side), including 1 transverse scan sequence of the common carotid through the bulb and 5 longitudinal images taken from both the right and left carotid arteries for each subject. Each of these images was collected in a specified order and recorded. The digitized data were batched and mailed on magneto-optical disks to the Reading Center at Wake Forest University for wall-thickness measurements.

Cardiac CT scans were performed using a gated-cardiac electron-beam CT scanner. At UCSF, the system was either the 16D scanner (Philips Medical Systems, Andover, MA) or the MSD Aquilion 64 model (Toshiba Medical Systems, Tustin, CA). At NWU, the technicians used the Sensation Cardiac 64 Scanner (Siemens Medical Solutions, Malvern, PA). Participants were examined in the supine position, placed in the scanner head first, with both arms raised above the head. A 4-sample calibration phantom provided on loan by the MESA CT reading center was placed under the thorax for each study. A scout image was done to determine the level of the carina, and the first scan was set at exactly 1 cm below the carina. Scanning was performed from superior to inferior, and a total of 46 images were obtained with 3.0-mm slice thickness. Exposures was set at 140 kV and 50 mAs for participants weighing ≤ 100 kg. For participants weighing >100 kg, the mAs was set at 63. Reconstruction was done in the 35-cm field of view. All CT scans were sent in batches to the Reading Center at Harbor-UCLA Medical Center, where they were read with Rephot Imaging software according to the MESA study methods.

After completing the cardiac CT scan, the technician used a lateral scout image of the spine to establish the

correct position (between the L4 and L5 vertebrae) for the abdominal CT using standardized protocols. Visceral fat and subcutaneous abdominal fat were scanned at the L4-L5 level after participants were positioned supine with their arms above their head and legs elevated with a cushion to reduce the spinal curvature. All CT scans were digitally recorded and sent to the Coordinating Center for future batched readings. The abdominal CT cuts will be used to calculate the visceral, subcutaneous, and intermuscular adipose tissue compartments using Medical Image Processing, Analysis and Visualization (MIPAV) software from the National Institute on Aging of the National Institutes of Health.

Subclinical Atherosclerosis Prevalence and Minimum Detectable Effects

To determine a sample size that has adequate power to detect small to moderate associations for our main study objectives, we determined the minimum detectable effects over a range of sample sizes. With a sample size of 900, descriptive statistics for the South Asian sample will be precise: margins of sampling error (MSEs; ie, half-width of 95% confidence intervals) for binary characteristics will be 1.4 to 3.3 percentage points, depending on prevalence, whereas MSEs for the means of continuous variables will be only 0.07 standard deviation (SD). In interethnic comparisons of cIMT by sex and other binary predictors, we will have 80% power to detect differences of 0.04 to 0.05 mm, depending on the proportions in each race/ethnic group. For CAC scores, minimum detectable relative between-ethnic group differences will be 57% to 75%. With a sample size of 900, we will also have 80% power to detect adjusted correlations of both these outcomes with continuous predictors as small as 0.1. In examining interactions between continuous measures of diet, exercise, and acculturation, we will have 80% power to detect adjusted correlations of approximately 0.1 between the product term capturing the interaction and cIMT or log coronary artery calcium (CAC), a reasonably small effect. In a logistic model for CAC scores ≥ 10 , which are expected in approximately 40% of the sample based on the MASALA pilot study results, we will have 80% power to detect odds ratios (ORs) of 1.22 per SD increase in continuous predictors, and ORs of 1.51 to 1.67 for binary predictors, depending on their prevalence; these ORs correspond to between-group adjusted differences in outcome prevalence of 10 to 13 percentage points. Minimum detectable ORs in the proposed ordinal models for categorized CAC should be smaller.

Cohort Surveillance and Follow-up for Events

At approximately 12 months and 24 months after the baseline examination, follow-up contacts are being conducted with each participant. These contacts will comprise a telephone interview and a mailed or emailed questionnaire. Any affirmative answers to preliminary queries about new medical conditions will be followed up by a telephone interview to complete an additional, more detailed questionnaire specific to the type of event that the participant reported. The additional questionnaire will gather information on hospitalizations, treatments, and lifestyle changes recently instituted. Any reported incident

CVD events or hospitalizations will be followed up with a request for their medical records. We will obtain participant consent for release of these health records. Data from these records will be abstracted by trained professionals and transmitted securely to the Coordinating Center. An independent expert review panel will adjudicate any incident cardiovascular events. These procedures are similar to follow-up methods used in the MESA study.

The aggregate CVD outcome will include CHD (definite and probable MI, definite CHD death, resuscitated cardiac arrest, definite angina, and probable angina associated with coronary revascularization), stroke (fatal or nonfatal), and other atherosclerotic CVD death. An independent cardiologist on our centralized adjudication committee will classify MI as definite, probable, or absent, based primarily on combinations of symptoms, ECG, and cardiac biomarker levels. Reviewers will grade angina, based on their clinical judgment, as definite, probable, or absent. They will classify CHD or CVD death as present or absent based on hospital records and interviews with families. Definite fatal CHD will require an MI within 28 days of death, chest pain within the 72 hours before death, or a history of CHD and the absence of a known nonatherosclerotic or noncardiac cause of death. A neurologist will classify stroke if there was a focal neurologic deficit lasting 24 hours or until death with a clinically relevant lesion on brain imaging and no nonvascular cause. If there are any disagreements in events adjudication between the 2 assigned experts, a third independent physician adjudicator will review the medical records to break the tie.

Clinical CVD Estimated Incidence

We used the available longitudinal CHD mortality data^{10,11} and cross-sectional estimates of CVD death^{9,25} in South Asians, along with the current event rate for the White participants in MESA,²⁶ to estimate an aggregated CVD incidence for the MASALA participants. We also took under consideration that the pilot-study participants who would be included in the larger cohort would have a total of 6 to 7 years of cumulative follow-up. With these considerations, we estimated that 55 to 63 of the approximately 900 South Asians enrolled in the cohort will experience CVD events (MI, CHD death, resuscitated cardiac arrest, definite angina, probable angina associated with coronary revascularization, stroke [fatal or nonfatal], or other atherosclerotic CVD death) during the 2 years of follow-up. The minimal detectable relative hazard for continuous predictors will be 1.45 to 1.49 per SD increase in the predictor, depending on the number of events.

Quality Assurance and Control

Staff from both sites were centrally trained and certified for all procedures at the UCSF Coordinating Center (CC). Staff were trained on recruitment, conducting interviews, phlebotomy and specimen processing, blood pressure measurements, anthropometry, ECG, ultrasound and CT procedures, and data transmission and verification.

For all measures performed, we will follow the MESA protocol for all quality control. We will conduct 5% blind split samples for all laboratory assays to estimate technical

errors for assessing the laboratory quality. Intrareader and inter-reader variability for the CT scans and ultrasound readings will be assessed with 10% random rereading of scans.

Data Management

The CC designed machine-readable study questionnaires and the clinical sites completed the data forms and transmitted them to the CC using standard fax machines. At the CC, the data forms were received by an automated fax server that uses optical character recognition technology to acquire the data. The data forms were scanned using TeleForm software (Cardiff Software, Vista, CA). Once the forms arrived at the CC, they were "verified" on screen by a CC data manager. Verified data were sent over the local area network at the CC to a database on a Microsoft SQL server. The images of the questionnaires were stored in an image-management system on optical disk. Each night, all study data were subjected to a set of error-checking programs. These error routines include checks for completeness, data consistency, and invalid ranges. The results were posted to the study website. Clinical site personnel checked the website daily to confirm that the CC had received all of the faxed forms and to address errors that may be posted. The CC posted real-time reports on data quality on the website and distributed hardcopy reports quarterly to the Steering Committee.

Results

We mailed invitational letters and attempted to call a total of 9097 households (4273 at UCSF and 4824 at NWU). We could not reach any household members in 4036 (44%) households, even after a second mailing to those with reliable address information and multiple phone-call attempts. Another 2424 (27%) households had individuals who declined to speak with recruitment staff to determine eligibility. Staff reached 2637 (29%) households and determined eligibility on 3053 individuals (1.2 average enumerates per household). Table 2 shows the yield from our telephone-based recruitment efforts among the 3053 individuals reached. Approximately 41% of individuals were ineligible, with higher rates of ineligibility due to young age at the UCSF site and due to other ethnicity at the NWU site. Of those found to be eligible, approximately 19% were not interested in study participation (23% at UCSF and 12% at NWU). Another 10% of individuals were eligible but were not offered enrollment because the age/sex stratum was already filled. After excluding those who were ineligible and those not offered enrollment because of filled strata, the enrollment rate was 60.8% (52% at UCSF and 77% at NWU).

Over approximately 30 months of recruitment, we enrolled 906 participants in the MASALA study. Table 3 shows the basic demographic characteristics of the MASALA study cohort. Of the 496 participants enrolled at the UCSF site, half were women. Among UCSF enrollees, 115 had been participants in the MASALA pilot study cohort from 2006–2007 (77% retained from the 150 pilot-study participants); 3 of these participants were age 80 to 84 years at the time of enrollment in the current study.

Table 2. Telephone Recruitment Yield, MASALA Study, 2010–2013

	Overall	UCSF	NWU
Total households attempted to reach, n	9097	4273	4824
Total individuals reached, n	3053	2035	1018
Total ineligible among those reached	1252 (41.0)	822 (40.4)	430 (42.2)
Reasons for ineligibility			
Age	351 (11.5)	281 (13.8)	70 (6.9)
Ethnicity	459 (15.0)	259 (12.7)	200 (19.6)
Existing CVD	199 (6.5)	130 (6.4)	69 (6.8)
Other exclusion criteria	243 (8.0)	152 (7.5)	91 (8.9)
Eligible but not interested	583 (19.1)	464 (22.8)	119 (11.7)
Eligible but stratum filled	312 (10.2)	253 (12.4)	59 (5.8)
Enrolled (of all found eligible)	906 (50.3)	496 (40.9)	410 (69.7)
Enrolled (eligible minus stratum filled)	906 (60.8)	496 (51.7)	410 (77.5)
Abbreviations: CVD, cardiovascular disease; MASALA, Mediators of Atherosclerosis in South Asians Living in America; NWU, Northwestern University; UCSF, University of California, San Francisco. Data are presented as n (%) unless otherwise indicated.			

The NWU site enrolled a total of 410 participants, with a higher proportion of men (58%). Overall, 98% of study participants were immigrants who had lived in the United States for an average of 27 ± 11 years. A majority of participants were born in India (84%), with the second most common country of birth being Pakistan (5%). There were significantly more immigrants from Pakistan recruited at the NWU site compared with UCSF, and there were more immigrants from the Fiji Islands at the UCSF site compared with NWU.

Only 4% of all clinical examinations were conducted in Hindi or Urdu; a higher proportion of women than men completed the examination visits in a South Asian language (7% vs 2%, $P = 0.002$). There was high educational attainment in this cohort, with approximately 88% of participants reporting education level of a bachelor's degree or higher. Family income was also high, with 63% of participants reporting annual household income $\geq \$100\,000$. These socioeconomic status (SES) indicators were high at both sites, but South Asians at the UCSF site had higher socioeconomic attainment than did South Asians at the NWU site.

Discussion

The MASALA study will provide novel data on the prevalence and associations of cardiovascular risk factors and subclinical atherosclerosis in South Asians, a rapidly growing segment of the US population with previously reported high risk of cardiometabolic risk factors and CVD. This study has been modeled on the MESA study, and

Table 3. Baseline Characteristics of the MASALA Study Participants by Site, 2010–2013^a

	Overall, N = 906	UCSF, n = 496	NWU, n = 410	P Value
Sex, F	420 (46)	248 (50)	172 (42)	0.02
Age, y	55 ± 9	55 ± 9	55 ± 9	0.94
40–49 years	293 (32)	159 (32)	134 (33)	
50–59 years	301 (33)	168 (34)	134 (33)	
60–69 years	236 (26)	127 (26)	108 (26)	
70–84 years	76 (8)	42 (8)	34 (8)	
Language used during clinical visit was Hindi or Urdu	39 (4)	21 (4)	18 (4)	0.91
Immigrants to the United States	887 (98)	490 (99)	397 (97)	0.04
Years lived in the United States ^a	27 ± 11	27 ± 11	27 ± 11	0.61
0–10	52 (6)	24 (5)	28 (7)	
11–20	225 (25)	131 (27)	94 (24)	
21–30	257 (29)	143 (29)	114 (29)	
31–40	242 (27)	131 (27)	111 (28)	
≥ 40	111 (12)	61 (12)	50 (13)	
Birth country				<0.001
India	757 (84)	418 (84)	339 (83)	
Pakistan	41 (5)	13 (3)	28 (7)	
Nepal	4 (<1)	2 (<1)	2 (1)	
Sri Lanka	9 (1)	6 (1)	3 (1)	
Bangladesh	5 (1)	2 (<1)	3 (1)	
Burma/Myanmar	5 (1)	1 (<1)	4 (1)	
United States	19 (2)	6 (1)	13 (3)	
Sub-Saharan Africa	27 (3)	16 (3)	11 (3)	
Fiji Islands	17 (2)	17 (3)	0	
Other Diaspora country	22 (2)	15 (3)	7 (2)	
Highest educational attainment				0.05
Lower than high school	61 (7)	30 (6)	31 (8)	
Lower than bachelor's degree	49 (5)	23 (5)	26 (6)	
Bachelor's degree	261 (29)	130 (26)	131 (32)	
Higher than bachelor's degree	535 (59)	313 (63)	222 (54)	
Family income				<0.001
<\$40 000	115 (13)	39 (8)	76 (19)	

Table 3. Continued

	Overall, N = 906	UCSF, n = 496	NWU, n = 410	P Value
\$40 000–\$75 000	120 (14)	59 (12)	61 (15)	
\$75 000–\$100 000	89 (10)	44 (9)	45 (11)	
≥\$100 000	556 (63)	342 (71)	214 (54)	

Abbreviations: MASALA, Mediators of Atherosclerosis in South Asians Living in America; NWU, Northwestern University; UCSF, University of California, San Francisco.
Data are presented as n (%) or mean ± SD.
^aAmong those who were US immigrants.

a major strength is the ability to compare risk-factor and atherosclerosis prevalence and correlates to the 4 MESA ethnic groups. The baseline study visit has been completed to establish the cohort, and annual telephone follow-up has been started to accumulate data on clinical CVD endpoints.

The characteristics of the MASALA cohort appear to be grossly representative of the middle-age to older-age South Asian population that currently resides in the United States, despite the high noncontact rate from our invitational letters and phone recruitment. According to the 2010 US Census, a majority of 3.4 million South Asians reported Asian Indian ethnicity (2.8 million; 83%).¹ However, the MASALA cohort includes a lower proportion of Pakistani individuals (5% in MASALA vs 10.6% in the 2010 Census) and a higher proportion of Bangladeshis and Sri Lankans than in the US Census. The small number of South Asians from countries other than India in this cohort will make it difficult to examine the effect of nationality on risk factors or outcomes.

The high socioeconomic attainment observed among South Asians in the MASALA cohort is consistent with national survey data. According to recent American Community Survey estimates, the proportion of Asian Indians with educational attainment of a bachelor's degree or higher was 69%, and the median family income was \$102 059.²⁷ However, it is possible that some of the nonresponders or those who declined to participate in MASALA were of lower SES, had language barriers, or were more recent immigrants. Because we have few participants in lower SES or educational-attainment categories, we will have limited ability to directly examine the effect of lower SES on disease associations. The higher educational attainment and SES of the MASALA study population may limit the generalizability of the study findings to all South Asians of lower SES within the United States and to all South Asians globally.

Reasons for the high socioeconomic attainment in US South Asians can be attributed in large part to immigration patterns. Immigration to the United States from South Asian countries was very limited prior to the Immigration and Nationality Act (Hart-Celler Act) of 1965.²⁸ This act restricted immigration from the Eastern Hemisphere to family members of US citizens and permanent residents, professionals and scientists, and workers in occupations for which labor was in short supply in the United States. As a

result, early immigrants from South Asian countries were primarily those seeking higher education or professionals, reflected in the relatively high SES of South Asians in the United States currently and among those in the MASALA cohort, who have an average of 27 years since immigration. There is a distinct contrast between the relatively recent and higher-SES South Asian immigrants in the United States and immigrants to the United Kingdom and other Diaspora countries; those immigrations occurred much earlier in time and consisted of seaman, skilled and unskilled laborers, and fewer educated individuals. The MASALA cohort provides an opportunity for understanding CVD risk factors and progression in this high-risk ethnic group through the lens of immigration and higher SES in comparison with other contemporary studies of South Asians in native²⁹ and Diaspora settings.^{30,31}

Future follow-up clinical examinations have been proposed and will continue to follow CVD endpoints. Long-term follow-up of this cohort will be able to determine whether CVD risk prediction is similar among South Asians as in other ethnic groups, a question that has not been answered by other existing studies.

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