Population Study of Urban, Rural, and Semiurban Regions for the Detection of Endovascular Disease and Prevalence of Risk Factors and Holistic Intervention Study (PURSE-HIS)

Rationale, Study Design, and Baseline Characteristics

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ABSTRACT

We designed and implemented the PURSE-HIS (Population Study of Urban, Rural and Semiurban Regions for the Detection of Endovascular Disease and Prevalence of Risk Factors and Holistic Intervention Study) to understand the prevalence and progression of subclinical and overt endovascular disease (EVD) and its risk factors in urban, semirural, and rural communities in South India. The study is also designed to generate clinical evidence for effective, affordable, and sustainable community-specific intervention strategies to control risks factors for EVD. As of June 2012, 8,080 (urban: 2,221; semirural: 2,821; rural: 3,038) participants >20 years of age were recruited using 2-stage cluster sampling. Baseline measurements included standard cardiovascular disease risk factors, sociodemographic factors, lifestyle habits, psychosocial factors, and nutritional assessment. Fasting blood samples were assayed for putative biochemical risk factors and urine samples for microalbuminuria. All nondiabetic participants underwent oral glucose tolerance test with blood and urine samples collected every 30 min for 2 h. Additional baseline measurements included flow-mediated brachial artery endothelial vasodilation, assessment of carotid intimal medial wall thickness using ultrasonography, screening for peripheral vascular disease using ankle and brachial blood pressures, hemodynamic screening using a high-fidelity applanation tonometry to measure central blood pressure parameters, and aortic pulse wave velocity. To assess prevalence of coronary artery disease, all participants underwent surface electrocardiography and documentation of ventricular wall motion abnormality and function using echocardiography imaging. To detect subclinical lesions, all eligible participants completed an exercise treadmill test. Prospectively, the study will assess progression of subclinical and overt EVD, including risk factor–outcome relationship differences across communities. The study will also evaluate community-specific EVD prevention using traditional Indian system of medicine versus recognized allopathic (mainstream) systems of medicine.

Endovascular diseases (EVD), comprising coronary artery disease (CAD), cerebrovascular disease, and peripheral vascular diseases, are the number one cause of death worldwide [1]. An estimated 17.3 million people died from EVD (mainly heart disease and stroke) in 2008, and this number is projected to reach 23.3 million by 2030 [1,2]. Developing, low-, and middle-income countries are disproportionately affected and account for >80% of EVD deaths that take place worldwide [1].

There are significant gaps in the knowledge of the epidemiology and associated risk factors of EVD in countries in the South Asian region, particularly India. Mortality data collected hitherto have been inadequate, and there is little information on regional variations in EVD incidence and mortality. Based on the Global Status on Non-Communicable Diseases Report, there were >2.5 million deaths from EVD in India in 2008, two-thirds of which were due to CAD [1].

There have been no national studies to evaluate the incidence and prevalence of CAD in India. Current estimates of the CAD burden are based on multiple ad hoc population-based cross-sectional surveys performed in urban or rural populations over the past 60 years [3]. These studies are limited by small and variable sample sizes, inconsistent and poor response rates, use of inappropriate diagnostic criteria, lack of age standardization, and incomplete reporting of results [3,4]. Moreover, because these studies have not identified patients with silent and asymptomatic (subclinical) CAD disease [5], the actual prevalence of CAD may be much higher than the reported prevalence of 6.5% and 13.2% in urban settings [6–11] and between 1.6% and 7.4% in rural India [10,12–15]. Epidemiological studies on stroke and other cerebrovascular diseases, and on the overall prevalence of peripheral vascular diseases in India are also few and suffer from the limitations listed for CAD [3,16–20].
Estimates suggest that the incidence and prevalence of EVD and its risk factors are increasing, and it is estimated that EVD will emerge as the main cause of death in India [21–27]. This situation may reflect rapid shifts in demographics with urbanization of the population and globalization of unhealthy lifestyle. Studies estimating clustering of risk factors both at the individual and at the urban and rural community level are lacking. Furthermore, risk factors in a population that is rapidly transitioning from rural to urban, defined as semiurban, have not been estimated.

Those with EVD in India tend to be younger, with 52% of cardiovascular deaths occurring before the age of 70 years compared with just 23% in more developed countries [28]. This has major socioeconomic consequences [29]. The development and implementation of effective, low-cost preventive measures and treatment strategies are public health priorities [30]. There is now a good understanding of the methodology involved in implementing EVD prevention programs in developed countries. However, in resource-challenged settings, such as India, data on which to plan and implement EVD prevention protocols are lacking. The fundamental principles for EVD prevention are likely to be similar across diverse populations [31], but the practicalities of implementation in different health care systems and contexts can vary greatly.

In India, the conventional (Western or allopathic) system of medicine coexists with traditional forms of medicine. Traditional systems include ayurveda, siddha, and unani systems, combined with yoga, naturopathy, and homeopathy. These traditional systems are widely used, particularly in rural areas that are home to nearly 70% of the Indian population [32]. Nearly 50% of the registered medical practitioners in India have formal training in 1 of the Indian traditional systems of medicine and a majority of them practice in rural areas [33]. Many of the traditional systems of medicine are recognized and regulated by the Government of India and are part of the national health care system [34]. However, the traditional system of medicine is not always well integrated with allopathic medicine practice, particularly in allopathic hospitals [35,36].

Allopathic medicine predominates in the treatment of EVD in India. However, health care costs, the lack of allopathic doctors and awareness of side effects reduce access and compliance in the treatment of EVD [37,38]. Siddha medicine, one of the oldest systems of medicine in India and prevalent mainly in Southern parts of India, may offer a cost-effective alternative or adjuvant to mainstream medicine [39,40]. Allopathy, in combination with siddha and lifestyle modifications, could emerge as the ideal holistic interventional strategy for the prevention of EVD in the Indian setting [40,41]. Despite the promise held by such novel interventional strategies, studies on integrated strategies have not yet been conducted.

Two areas require immediate attention. The first is the need of generating valid estimates of both risk factors and the huge iceberg of subclinical EVD that is, as yet, unidentified and therefore untreated. The second is the introduction and integration of a culturally accepted alternative system of medicine with mainstream allopathic medicine to produce a comprehensive system for preventing EVD.

With this background, we designed a cohort study, the PURSE-HIS (Population Study of Urban, Rural and Semiurban Regions for the Detection of Endovascular Disease and Prevalence of Risk Factors and Holistic Intervention Study) in Tamil Nadu, India. The study was designed to meet the following objectives: 1) to estimate the prevalence of risk factors for EVD among the urban, semiurban, and rural communities; 2) to estimate the prevalence of overt EVD in urban, semiurban, and rural communities; 3) to estimate the prevalence of subclinical EVD by provocative testing in urban, semiurban, and rural communities; 4) to estimate the progression of subclinical and overt EVD in these communities, including an examination of how the risk factor–outcome associations vary across communities; and 5) to develop, implement, and evaluate EVD prevention strategies with an alternative system of medicine and/or with a recognized allopathic system of medicine.

MATERIALS AND METHODS
Study design
We used a cross-sectional design to estimate the prevalence of risk factors, biomarkers, subclinical EVD, and overt EVD at baseline. The prospective cohort design makes it possible to determine the impact of holistic interventions on risk factors and on the course of EVD.

Study setting
We selected 3 distinct populations in regions defined as urban, semiurban, or rural, as based on the 2001 Indian Census. The urban area subjects were drawn from Chennai, the capital city, and the semiurban and rural area subjects were selected from Thiruvallur and Kanchipuram districts, respectively, in the state of Tamil Nadu, India.

Sampling
We used a 2-stage cluster sampling method in urban, semiurban, and rural areas. In the urban setting, the primary sampling unit was that of urban administrative units (divisions). In the first stage, we selected 9 of 155 divisions, and in the second stage, the required number of clusters (streets) was selected by simple random sampling. In the semiurban region, the primary sampling unit was that of the village-level administrative units (town panchayats). We selected 9 of 37 town panchayats, and the required number of clusters (wards) was selected by simple random sampling. In rural regions, the primary sampling unit was that of rural administrative areas (blocks). We selected 5 of 27 blocks and the required number of clusters (village panchayats) by simple random sampling. If the selected
cluster was small, the immediate neighboring area of the selected cluster was included until the target sample size was achieved.

**Study population**

An individual house was the sampling unit. All members of the household >20 years of age without documented evidence of carcinoma, severe psychiatric illness, stage IV cardiac failure, or human immunodeficiency virus infection were included in the study.

**Sample sizes**

We set power at 80%, and alpha at 5% and assumed 20% nonresponse and a design effect of 2. We recruited 2,221 subjects from the urban area and 3,038 from rural areas, on the basis of assumptions of prevalence of CAD (10% in urban and 7% in rural areas). Because the semiurban area was between the urban and rural areas, both in terms of location and socioeconomic development, we assumed an average of the sample sizes that were required for urban and rural areas (n = 2,821).

**Subject recruitment and data collection**

The study was approved by the Institutional Ethics Committee (IEC-06/53/47) at Sri Ramachandra University, Chennai, India, and was registered with Clinical Trials Registry, India (CTRI/2011/04/001677). Figure 1 describes the study protocol and subject flow. At the field level, during the enumeration process detailed in previous sections, we explained the objective of PURSE-HIS study, the test procedures, benefits, and risks to the participants, and obtained informed written consent. During the home visit, we obtained detailed demographic information by an interviewer-administered questionnaire using structured instruments, which included information on the type of housing, water source, education and income levels, type of work, caste, and religion. At the end of the survey, participants were given a date for their visit to the study center and were advised to come after fasting overnight. On the date of appointment, the participants were transported to the study center located in the University Hospital at Sri Ramachandra University, Chennai, India. Fasting blood specimens were collected in 4 different vacuum containers, and urine samples were collected in sterile plastic containers for various assays. All nondiabetic participants were given 75 g of glucose dissolved in 250 to 300 ml water and an oral glucose tolerance test was conducted. The blood and urine specimens were collected every half hour for up to 2 h. For diabetic subjects, a standard breakfast was provided and blood and urine specimens were collected after 2 h for post-prandial sugar readings. All blood and urine samples were transported to the accredited central biochemical laboratory for the biochemical investigations listed in Table 1.

**Clinical examination by allopathic system**

An interviewer-administered questionnaire was used to collect data on EVD and risk factors. After a general clinical examination, seated blood pressure (BP) of participants was measured in the dominant arm using validated automated oscillometric BP device Omron Sem-1 (Omron Healthcare, Singapore) with an appropriate bladder size. Three readings were taken and the mean was used in the analysis.

**Clinical examination by siddha medical system**

A detailed clinical evaluation was performed in accordance with the siddha system to ascertain madhumegam (diabetes mellitus), pitkadhibbham (hypertension), adhi harudhi kozhuppam (dyslipidemia), and thanamaraga noi (coronary artery disease) among the participants. The siddha physician examined the participants using siddha clinical examination procedures of envagai thervugal (8 ways of examination), vannai (immunity), gunam (character), czhu udal kattugal (7 body constituents), udal vagai (body type), and naadi (pulse).

**Anthropometric, physical activity, nutritional status, and psychosocial stress assessments**

Anthropometry (height, weight, waist, hip circumference, and skin-fold thickness at 5 sites) data were collected for all participants. The body fat percentage was measured using the bioelectric impedance automated Omron body fat analyzer HBF-306 model (Omron Healthcare). Nutritional status of all participants was assessed using a 24-h recall of food intake and a food frequency questionnaire [42]. Physical activity was measured by a physiotherapist using the Global Physical Activity Questionnaire [43]. A clinical psychologist assessed the level of stress, anxiety, and depression using the Presumptive Stressful Life Event Scale [44], Hamilton Anxiety Rating Scale [45], and Hamilton Depression Rating Scale [46] respectively.

**Subclinical EVD evaluation**

Developments in the measurement of cardiovascular structure and function have made imaging of subclinical disease in population-based studies feasible and accurate. The PURSE-HIS study was built on successful subclinical epidemiologic studies that have included objective measures of subclinical EVD [47].

**Electrocardiography.** Resting 12-lead electrocardiography recordings (Mortara ELI 250c, Mortara Instrument, Milwaukee, WI, USA) were obtained in supine position and read using the Minnesota code [48].

**Central pressure and arterial stiffness analysis.** Radial artery waveforms were recorded with a high-fidelity micromanometer (SPC-301, Millar Instruments, Houston, TX, USA) from the wrist of the dominant arm. Pulse wave analysis (SphygmoCor, AtCor Medical, West Ryde, New South Wales,
PURSE-HIS Cohort
Urban (n=2221; Semi-urban (n=2821); Rural (n=3038)

Home visit
Study explanation and written informed consent;
Allocation of unique ID;
Collect demographic data

Transportation to the study center

Fasting blood and urine samples to assay biochemical risk factors;
Clinical history & examination

Oral glucose tolerance test
Known diabetic?
No
Yes
Postprandial blood sugar

Anthropometric, nutritional & psychosocial assessments

Electrocardiography, Echocardiogram, Flow mediated dilatation of brachial artery,
Carotid intima medial thickness, Central pressure and arterial stiffness and ankle brachial index assessments

Modified Bruce protocol – treadmill test
Cardiac abnormality?
Yes
No
Bruce protocol – treadmill test

Meet inclusion/exclusion criteria?
Yes
Holistic intervention
No
Routine follow up

FIGURE 1. Subject recruitment, baseline survey, sample collection, and cohort follow-up for the PURSE-HIS (Population Study of Urban, Rural and Semiurban Regions for the Detection of Endovascular Disease and Prevalence of Risk Factors and Holistic Intervention Study).
TABLE 1. Biochemical investigations: PURSE-HIS study, South India

<table>
<thead>
<tr>
<th>Investigations</th>
<th>Method of Specimen Collection</th>
<th>Analytical Method/Instrument</th>
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<tbody>
<tr>
<td>Blood glucose</td>
<td>NA$_2$EDTA/sodium nitroprusside vacutainer</td>
<td>Dimention RXL Clinical Chemistry system (Bio-Rad, Hercules, CA, USA), with kits from Siemens (Washington, DC, USA)</td>
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<tr>
<td>Lipid profile*</td>
<td>Serum separator gel-vacutainer</td>
<td>Dimention RXL Clinical Chemistry system with kits from Siemens</td>
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<tr>
<td>Liver function test</td>
<td>Serum separator gel-vacutainer</td>
<td>Dimention RXL Clinical Chemistry system with kits from Siemens</td>
</tr>
<tr>
<td>Renal function test</td>
<td>Serum separator gel-vacutainer</td>
<td>Dimention RXL Clinical Chemistry system with kits from Siemens</td>
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<tr>
<td>Thyroid-stimulating hormone</td>
<td>Serum separator gel-vacutainer</td>
<td>Chemiluminescence immunoassay, ADVIA Centaur (Siemens)</td>
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<tr>
<td>High-sensitivity C reactive protein</td>
<td>Serum separator gel-vacutainer</td>
<td>Immunonephelometry, BN ProSpec System (Bio-Rad) with reagents (Siemens)</td>
</tr>
<tr>
<td>Lipoprotein (a), apolipoprotein A-1 and B</td>
<td>Serum separator gel-vacutainer</td>
<td>Immunonephelometry BN ProSpec System</td>
</tr>
<tr>
<td>Homocysteine</td>
<td>EDTA-vacutainer</td>
<td>Fluorescence polarization immunoassay, AxSYM System and Kits (Abbott, Ludwigshafen, Germany)</td>
</tr>
<tr>
<td>Fasting insulin</td>
<td>EDTA-vacutainer</td>
<td>Microparticle enzyme immunoassay, AxSYM System</td>
</tr>
<tr>
<td>Hemoglobin A$_1c$</td>
<td>EDTA-vacutainer</td>
<td>HPLC, Bio-Rad D-10 HbA$_1c$ analyzer</td>
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<td>Routine hematology*</td>
<td>EDTA-vacutainer</td>
<td>Mindray S500 hematometry analyzer (Mindray, Shenzhen, China)</td>
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<tr>
<td>ESR</td>
<td>Sodium citrate-vacutainer</td>
<td>Ves-Matic 20 ESR analyzer (Diosset Diagnostica Senese S.p.A., Milano, Italy)</td>
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<tr>
<td>Urine analysis</td>
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<tr>
<td>Urine creatinine</td>
<td>Sterile plastic container</td>
<td>Konelab 60i (Thermo Fisher Scientific, Waltham, MA, USA) and reagents from Randox Laboratories (Antrim, Northern Ireland, UK)</td>
</tr>
<tr>
<td>Microalbumin</td>
<td>Sterile plastic container</td>
<td>Immunoturbidity, Konelab 60i and reagents from Randox</td>
</tr>
<tr>
<td>Routine urine analysis$^{**}$</td>
<td>Sterile plastic container</td>
<td>CLINITEK Advantus urine analyzer (Siemens)</td>
</tr>
</tbody>
</table>

 EDTA, ethylenediamine tetraacetic acid; ESR, erythrocyte sedimentation rate; HbA$_1c$, glycosylated hemoglobin; HPLC, high-performance liquid chromatography; PURSE-HIS, Population Study of Urban, Rural and Semiurban Regions for the Detection of Endovascular Disease and Prevalence of Risk Factors and Holistic Intervention Study.

*Includes total cholesterol, triglycerides, high-density lipoprotein, low-density lipoprotein.

$^{**}$Includes total protein, albumin, total bilirubin, direct bilirubin, serum glutamic oxaloacetic transaminase, serum glutamic pyruvic transaminase, and alkaline phosphatase.

$^{**}$Includes body urea nitrogen, serum creatinine, uric acid.

$^{**}$Includes red blood cell count; total leucocyte, polymorphonuclear leucocyte, eosinophil, monocyte basophil and lymphocyte cell counts; hemoglobin; and packed cell volume.

$^{**}$Includes color, pH, protein, specific gravity, bilirubin, glucose, ketone, urobilinogen, sediments, pus cells, red blood cells, epithelial cells, and casts.

Australia) was then used to generate a corresponding central (ascending aortic) waveform using a generalized transfer function [49], which has been prospectively validated for the assessment of ascending aortic BP [50]. Using the integral software, augmented pressure was calculated as the difference between the second and first systolic peaks. Augmentation index was calculated as augmented pressure expressed as a percentage of the pulse pressure. Heart rate was determined from the aortic waveform, and mean arterial pressure was obtained by integration of the waveform. The aortic pulse wave velocity was measured using the same device by sequentially recording electrocardiography-gated carotid and femoral artery waveforms [51]. Path length for the determination of aortic pulse wave velocity was measured as the surface distance between the suprasternal notch and femoral site minus the distance between the suprasternal notch and carotid site using a tape measure. All measurements were made in duplicate by trained investigators. Every hundredth tracing of tonometer assessment of radial artery pressure curve and derived central aortic pressures was transmitted to the reference vascular lab at Cambridge University, UK, to ensure the quality of the tracings.

**Doppler echocardiography.** All echocardiography imaging was performed according to the American Echocardiographic Association standardized protocols by registered diagnostic cardiac sonographers, who used the same echocardiographic instrument (Envisor, Philips, Cleveland, OH, USA). Ejection fraction, wall motion abnormality, incompetency of mitral and tricuspid valves, presence or absence of aneurysm, and diastolic functions of both right and left ventricles for each participant were assessed according to American Echocardiographic Association standardized protocols [52].

**Carotid intimal medial thickness assessment.** Intimal medial thickness of right and left common carotid arteries at the level of bifurcation were measured with participants in supine position, using a high-resolution B-mode ultrasonography system with linear transducer frequency of 7.5 MHz (Envisor, Philips). The image captured was transferred to the computer and processed using the border detection program IntiMaTe 2.0 (Pixen, Chennai, India). A portion of carotid artery image was magnified 50x and intimal medial thickness was measured [53–55].

**Ankle-brachial index measurement.** The ankle-brachial index values were measured using the traditional continuous wave Doppler of Versalab Dx (Diabetik Foot Care India, Chennai, India) and oscillometric sphygmomanometer.
(Welch Allyn, Skaneateles Falls, NY, USA). All ankle-brachial index measurements were performed with the subjects in supine position. To obtain the ankle-brachial blood pressure index, blood pressure was measured with a Doppler probe in the bilateral brachial, dorsalis pedis, and posterior tibial arteries [56]. The higher of the pressures obtained in the same ankle was used as the numerator for the ankle-brachial blood pressure index for that leg.

**Flow-mediated dilation of the brachial artery.** Flow-mediated dilation (FMD) of the left brachial artery was measured using high-resolution-B mode ultrasonography system (Envisor) with a linear transducer frequency of 12.5 MHz and an oscillometric sphygmomanometer (Welch Allyn) in supine position. The brachial artery flow and diameter were measured at rest. To determine the diameter immediately after reactive dilation induced by ischemia, the cuff was wrapped around the left forearm, inflated 50 mmHg above the systolic BP of the participant, kept inflated for 5 min, and then deflated. After cuff release, maximum peak flow velocity was measured within 15 s and arterial diameter at 45, 90, 180, and 300 s. Percentage of flow-mediated dilation ([peak diameter − baseline diameter]/baseline diameter) was used for analysis [57]. The reproducibility of flow-mediated dilation was assessed (n = 100). Intra-observer reliability yielded an intraclass correlation coefficient of 0.97 with a variation of <5%.

**Exercise treadmill test.** After excluding participants with contraindications through clinical examination and echocardiography, the treadmill test was performed on all other participants. An X-Scribe II Stress Exercise System (Mortara Instruments) with in-built Bruce protocol was used for this test. The American College of Cardiology/American Heart Association 2002 Guideline Update was followed for exercise testing. A modified Bruce protocol was used in case of grade II obesity, pain in lower limb, respiratory impairment, post-myocardial infarction or coronary artery bypass graft, and minor physical handicaps [58].

**Quality control**

The study staff was trained and demonstrated competency in relevant procedures before being certified to perform procedures for the PURSE-HIS study. This included interviews, phlebotomy and specimen processing, all BP measurements, anthropometry, electrocardiography, vascular imaging and Doppler studies, collection of arterial waveforms, echocardiography, treadmill stress test, and data entry. Quality control checks were performed, and the instruments were calibrated according to protocols recommended by the manufacturer. Experts from the National Institute of Epidemiology, Government of India, New Delhi, spent 1 month at the study center and independently validated the study procedures. As part of the validation process, the team inspected infrastructure facilities and instruments used in the study. They tested the clinical knowledge and communication skills of the study team. This was followed by observation of the team members in the conduct of the study protocol.

**Operational definition of risk factors and EVD**

Diabetes mellitus, hypertension, and dyslipidemia were defined based on World Health Organization criteria [59], Seventh Report of the Joint National Committee on the Prevention, Detection, Evaluation, and Treatment of High Blood Pressure criteria [60], and National Cholesterol Education Program guidelines [61], respectively. CAD was defined based on history of myocardial infarction or hospitalization for treatment of unstable angina, angina pectoris corroborated by objective evidence of myocardial ischemia, history of coronary revascularization or angiographic evidence of stenosis > 75% in ≥ 1 major epicardial coronary arteries, presence of an abnormal resting electrocardiogram suggestive of ischemic heart disease, positive stress test, and wall motion abnormalities detected by echocardiography. Cerebrovascular disease was defined by history of transient ischemic attacks or ischemic stroke, carotid artery disease as evidenced by a history carotid endarterectomy, angioplasty, or other cerebral revascularization and advanced (at least 60% stenosis) atherosclerosis in the common or internal carotid artery, or vertebral artery system documented by ultrasound. Peripheral arterial disease was defined by history of aortic aneurysm repair, aorto-iliac, femoral, or other arterial surgery or angioplasty performed to relieve lower limb ischemia, lower limb amputation performed due to complications of atherosclerotic disease, and ankle-brachial pressure index <0.9 or classical symptoms of claudication disease.

**Cohort surveillance and intervention subarm**

Subjects who had mild to moderate expression of risk factors without the evidence of subclinical or overt EVD were included in the interventional phase of the study after counseling and obtaining informed consent. The patients who met the inclusion criteria and were willing to participate in the intervention phase were randomized into 2 groups: those who received 1) “traditional medicine” or 2) “modern medicine” for the management of their risk factors. These subjects were advised on diet and lifestyle modifications and recalled after 6 weeks, at which time, the levels of uncontrolled risk factors were reassessed. Those with the presence of uncontrolled risk factors despite diet and lifestyle modifications were then prescribed medication according to the groups to which they belonged. Follow-up studies are being performed on these subjects and will continue for 3 years. During the follow-up visits, the specific parameters for control of risk factors will be studied. In addition, we will document adverse events and assess compliance.

Subjects who were identified as having severe expression of risk factors or subclinical or overt EVD were provided with detailed reports based on the assessment and specific diagnoses along with standard medical advice.
Any “alert” findings — indications of conditions that should be medically evaluated on an urgent basis — were reported to participants and their physicians by telephone as soon as they were identified. All the participants are being followed prospectively, and the study will evaluate the incidence of new onset type 2 diabetes mellitus, systemic hypertension, dyslipidemia, and the new onset of EVD in those with or without risk factors at the end of 3 years of study.

Data management
All study data are stored in a centralized password-protected computer database. Subjects in the database are identified only by their PURSE-HIS identification. Documents that contain identifying information and the key linking the names and codes are locked in a separate file cabinet. The third-party validation of the data integrity was performed by experts from the National Institute of Epidemiology, Government of India, New Delhi. With respect to accuracy of data entry, the National Institute of Epidemiology team compared hard and soft copies of data and found omission and error rates to be within acceptable levels.

RESULTS AND DISCUSSION
The recruitment for PURSE-HIS study has been completed. A total of 8,080 participants have consented to participate in the study. The urban, semiurban, and rural stratified cohort design is a unique feature and the major strength of the study, as it provides comparisons that may offer unique insights on the incidence of EVD between demographic and socioeconomic milieus. It has been suggested that the prevalence of cardiovascular disease and risk factors may increasingly become concentrated among low socioeconomic status (SES) groups in India [62] and other low- and middle-income countries [63], although the empirical evidence from India in support of this hypothesis remains limited until now [64]. Along with SES, the effects of belief systems and lifestyle practices based on caste system (in vogue in India for centuries) and different religious practices on the risk for EVD are currently unknown. The PURSE-HIS study will investigate the effect of SES, caste, and religion on prevalence and progression of EVD. The baseline characteristics of the PURSE-HIS cohort based on age, community, caste, religion, education, occupation, and overall SES class are shown in Table 2 [65].

In addition, the PURSE-HIS study will, for the first time in Indian population, provide important information about major dimensions of subclinical EVD, including cardiac structure; function and conditions of the aorta, coronary arteries, peripheral arteries; and generalized measures of vascular function and compliance. Assessment of biochemical and other cardiovascular risk factors in major pathophysiologic domains will complement these measures. The PURSE-HIS study will provide information on risk factor-outcome relationships; it also has the potential to identify new risk factors for EVD, thus increasing the ability to predict and prevent EVD in a South Asian population.

Another unique aspect of the PURSE-HIS study is the assessment, design, and implementation of population-specific EVD prevention strategies that integrate siddha medicine. Like ayurveda, siddha medicine accepts that the

<table>
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<th>TABLE 2. Selected characteristics of participants in the PURSE-HIS study</th>
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<td>Urban</td>
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<tr>
<td>Female</td>
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<td>Mean age and distribution, yrs</td>
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<td>50–59</td>
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<td>60+</td>
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<td>Religion</td>
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Values are percentages unless otherwise indicated.
*Based on modified Kuppuswamy classification [65].
physiological function of the body is mediated and maintained by 3 forces: vali (vatham); azhal (piththam); and aiyam (kapam). Any imbalance is said to result in diseases. The treatment in siddha is aimed at restoring the original balance of the 3 forces. Along with drug therapy, a notable characteristic of siddha treatment is the use of yoga sutras [39] that advocate changes in diet, controlled breathing, and intense meditation, as well as certain postures or exercises for psychosomatic harmony. The use of allopathic system of medicine for diagnosis, with combined treatment strategies that include dietary and lifestyle modifications based on siddha medicine could provide culturally acceptable and cost-effective, community-specific strategies for prevention of EVD among Indians with potential applications in other resource-limited areas of the world as well.

REFERENCES
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