# STUDY PROTOCOL

## Solan Surveillance Study

**Study protocol: Version 1.2** | 12 November 2013

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## Study Protocol

**Version 1.2** | 12 November 2013 -

**CENTRE FOR CHRONIC DISEASE CONTROL**

*Funding agency:*

***Medtronic Foundation***

***Sub-study: National Heart Lung and Blood Institute, National Institutes of Health, USA***

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# List of Abbreviation

| | |
|---|---|
| **BMI** | Body Mass Index |
| **BP** | Blood Pressure |
| **BRFSS** | Behavioural Risk Factor Surveillance System |
| **COE-CARRS** | Center of excellence- Center for Cardiometabolic Risk Reduction in South Asia |
| **CDC** | Centers for Disease Control and Prevention |
| **CEB** | Census Enumeration Blocks |
| **CHD** | Coronary Heart Disease |
| **CHF** | Congestive Heart Failure |
| **CKD** | Chronic Kidney Failure |
| **CMD** | Cardiometabolic Diseases |
| **CUPS** | Chennai Urban Population Study |
| **CURES** | Chennai Urban Rural Epidemiology Study |
| **CVD** | Cardiovascular Disease |
| **DM** | Diabetes Mellitus |
| **EQ-5D** | European Quality of Life 5 |
| **FPG** | Fasting Plasma Glucose |
| **HINTS** | Health Information National Trends Study |
| **HTN** | Hypertension |
| **IDSP** | Integrated Diseases Surveillance Project |
| **IRB** | Institutional Review Board |
| **KAP** | Knowledge, Attitudes, and Perceptions |
| **LMCI** | Low- and Middle-Income Countries |
| **MI** | Myocardial Infarction |
| **MONICA** | Multinational MONItoring of trends and determinants in CArdiovascular disease |
| **MOP** | Manual Of Operations |
| **NABL** | National Accreditation Board for testing and calibration Laboratories |
| **NCCD** | National Center for Chronic Diseases |
| **NCD** | Non Communicable Diseases |
| **NIH** | National Institutes of Health |
| **NPDCS** | National Program for Prevention and Control of Diabetes, CVD and Stroke |
| **PHFI** | Public Health Foundation of India |
| **PI** | Principal Investigators |
| **PVD** | Peripheral Vascular Disease |
| **QME** | Quality Monitoring and Evaluation |
| **SOP** | Standard Operating Procedures |
| **UA** | Unstable Angina |
| **WHO** | World Health Organization |

# I. Background

## I.i. Cardio-metabolic diseases (CMD)

Cardio-metabolic diseases include diabetes mellitus (DM), cardiovascular disease (CVD), kidney disease and common risk factors that underlie these conditions such as central obesity, insulin resistance, glucose intolerance, dyslipidemia, and hypertension. CMD are a growing public health problem worldwide which is gradually becoming a pandemic.[1] They are among the top ten most costly diseases, but they have the advantage of being predictable through identification of distal and intermediate risk factors and also preventable through changes in lifestyle particularly through healthy eating habits and regular physical activity.[1]

## I.ii. Cardio-metabolic disease burden

It is estimated that coronary heart disease (CHD), cerebrovascular disease, and diabetes together account for 30% of global mortality and 80% of these deaths occur in low- and middle-income countries (LMIC).[2-4] Diabetes commonly co-exists with obesity (both generalised and central), hypertension,[5] and lipid abnormalities (elevated triglycerides, low HDL-cholesterol, abnormal LDL-cholesterol sub-fractions) and is a central feature accelerating athero-thrombotic cardiovascular disease (CVD), it is the leading cause of adult-onset blindness, non-traumatic amputations and kidney failure worldwide. The addition of these inter-related risk factors and co-morbidities results in a multiplicative, rather than additive, amplification of risk of severe outcomes (such as CVD events, amputation, etc.) and mortality.[6]

Among Indians, diabetes, cardio-metabolic risk factors[7, 8] and events[9, 10] occur at younger ages and lower body mass indices (BMI) when compared to other ethnic groups,[10-23] and are rapidly increasing with socioeconomic and nutrition transitions.[4, 24-26] Asian Indians, as a group, are projected to account for between 40-60% of the global CVD burden within the next 10-15 years.[30] Furthermore, 35% of CVD-related deaths in India occur in those between 35-64 years of age as compared to only 12% in the U.S.[31]

Previously it was thought that CMDs were confined to affluent urban residents, but this paradigm is gradually shifting as these conditions are now increasingly prevalent in lower socioeconomic groups in South Asia,[32-34] and CVD is currently the leading cause of death in both urban *and* rural India.[26, 35] Projections suggest that India's national income losses over the decade up to 2015 will amount to US$ 267 billion due to cardiovascular and diabetes deaths alone;[36] of these, the economically active age range (25-64) will bear great morbidity and mortality resulting in loss of human capital and productivity, perpetuating poverty faced by many, and potentially stifling development.

### I.iii. Surveillance for the prevalence of CMD and their risk factors

Surveillance of risk factors and disease is an invaluable public health research tool for: monitoring population health status; guiding resource allocation and policy; identifying and prioritizing interventions for subpopulations at particular risk; identifying disparities in outcomes; planning and evaluation of health programs.[37,38] Given the elevated and growing cardio-metabolic risk in India, [7, 10, 13, 19, 23, 25, 26, 39-42] the importance of surveillance cannot be underestimated. Current assessments of surveillance efforts in the subcontinent, and indeed most developing countries,[43, 44] suggest large data deficits, vast state-wise heterogeneity and variable data quality, limiting the value of existing figures.

### I.iv. Existing Surveillance system and Gaps

Currently the major source of population level estimates of CMD risk factors, morbidity and mortality in India has been ad hoc surveys. These surveys can generally be characterized as state-specific, with small, often highly variable sample sizes, varying and often low response rates, with use of different diagnostic criteria, and limited by problems of sample design, lack of standardization, frequent measurement errors and incomplete reporting of results.[45] Recent initiatives by the Government of India have attempted to address these deficiencies through setting up a National Program for Prevention and Control of Diabetes, CVD and Stroke (NPDCS), an Integrated Diseases Surveillance Project (IDSP) at multiple sites, and establishing two other NCD risk factor surveillance projects.[46, 47] However, these systems fall short by failing to provide critical CMD-specific incidence and mortality data, measures of diet and physical activity, secular trends in risk factors, health service utilization, health care costs, and quality of care. The Sample Registration System of India, for example, relies on medically certified deaths which account for just 15% of total mortality and coverage is limited to institutional deaths in urban areas.[48] Thus India suffers from a fragmented, chaotic, public-private mix of health-care providers with little or non-existent documentation.

### I.v. Arguments for Surveillance Models

Justification for establishment of a well-designed, integrated surveillance system lies not only in helping align resource allocation with actual needs, but also broader themes[49, 50] which include:

a. -More extensive comprehension of the distribution and trends of determinants and disease outcomes, especially given the asymptomatic prolonged course of NCD risk factors, the risk of debilitating target organ damage and often fatal disease events, as well as ensuing health and socioeconomic burdens. This is accomplished by:

    1. -Investigating the determinants of disease prevention through early risk factor detection and control, spanning the spectrum of awareness, knowledge, attitudes,

and practice (lifestyle behaviors, health-seeking and utilization, as well as treatment adherence, and perceived quality of life);

2. -Capturing newly-diagnosed cases, events, recurrent disease and mortality as well as the distribution and determinants associated;

b. -Dynamic integration of information from multiple sources, improving case detection,[51] quality of individual chronic care delivery, health information infrastructure and the opportunity to increase accountability through regular audits and evaluating efficacy of prevention and control strategies;[52-55]

c. -Reducing long-term health expenditure through culmination of safe, effective prevention and care models lowering rates of target organ damage, first events, recurrent disease, disability and premature mortality.

Experiences with surveillance models in developed countries have varied according to the stage of health system maturity and economic development. The U.S., for example, has relied on nationally-representative surveys, focusing primarily on self-reported disease risk factors (National Health Interview Survey, Behavioral Risk Factor Surveillance System or BRFSS). In following trends in cardiovascular risk factors, only one survey (National Health And Nutrition Examination Surveys) now routinely collects laboratory samples.[49] Countries with socialized national health systems, like the UK and Canada, have publicly-funded, networked, routine data capturing registers, although use and auditing of these systems is inconsistent. Models in Australia and much of Europe are based on regular standardized quality of care evaluation, acquiring population characteristics as well as provision of performance indicators based on provider processes and patient outcomes.[49]

The lessons drawn from these experiences and the published literature[49, 50, 49] support the utilization of standardized models that are not reliant on self-reporting, such as the World Health Organization (WHO) STEPwise Approach to Surveillance.[50] An initial, uniform prototype of this nature can be used to overcome infrastructural deficits in low-resource settings, and the foundation created may help advocate for modernizing and scaling up surveillance efforts towards an ideal system (networked, electronic health recording registers with data integrated from primary care, hospital, laboratory and home monitoring settings).[51, 56]

**I.vi. Study partners and their strengths**

The Investigators of our study are Drs. **Dorairaj Prabhakaran** (Principal Investigator, CCDC), **Nikhil Tandon** (AIIMS), and **Ajay V S** (PHFI). The study will be coordinated by the Centre for Chronic Disease Control, New Delhi, India. The investigators are currently leading another surveillance study in urban Delhi, Chennai and Karachi using a similar protocol – The CARRS Surveillance Study. The expertise and learning from implementing the CARRS Surveillance Study will be an added benefit in implementing the proposed study.

### I.vii. Objectives of the study

*Primary objectives*

a. - To implement and evaluate a model surveillance system for CMDs and its risk factors in rural Solan, Himachal Pradesh

b. - To assess the prevalence of CMD risk factors and diseases among adults aged 20 years and above, permanently residing in well-defined rural communities in Solan, Himachal Pradesh

c. - Ascertain factors that influence knowledge, attitudes, and perceptions (KAP) of the sample population regarding CMD and their risk factors

*Secondary objective*

a. - Determine the incidence of intermediate risk factors (in previously risk-free individuals), new-onset complications, and the associated morbidity and mortality

b. - To derive cost and health-utilization indices which can be used to model projected burdens of CMD in order to formulate cost-effective and timely interventions

## II. Methodology

### II.i. Study design

While the primary study design for the surveillance model is cross-sectional, a cohort study design will be used to follow-up the participants for four years subsequent to the cross-sectional study. The cross-sectional study will assess the prevalence of CMDs and their risk factors while the pilot cohort study will estimate the incidence of morbidity and mortality associated with CMDs.

The **Cross-sectional study** will be the initial study conducted in 2012-2013 which will also form the baseline for the cohort study conducted in subsequent years. A repeat cross-sectional survey will be conducted in 2016-2017 and by recruiting an independent sample in the same study site to estimate the trend (over 4 years) in prevalence of CMDs and their risk factors.

The **Cohort study** will follow the cross-sectional study and will be conducted at two years interval during 2014-2015 and 2016-2017. With informed consent, subjects enrolled into the cross-sectional study will be followed up as a cohort for four years to measure the outcomes of interest.

*Outcomes of interest:*

i. - Anthropometric Changes
  a. - Weight
  b. - Waist Circumference
  c. - Skinfold Thickness
  d. - Body Fat

ii. Development of new-onset intermediate risk factors
    a. Hypertension
    b. Diabetes mellitus
    c. Dyslipidemia
iii. Incident morbidity
    a. Stroke
    b. MI
    c. CHF
    d. Chronic Stable Angina
    e. Chronic Kidney Disease
iv. Complication
    a. PVD
    b. Retinopathy
    c. Nephropathy
    d. Neuropathy
    e. Amputation
v. Health service utilization and costs
    a. Hospitalization
    b. Outpatient use
vi. Mortality
    a. All cause
    b. CMD-specific

**II.ii. Study site and settings**

The Surveillance study will be conducted in Solan District of Himachal Pradesh. This will be a household survey wherein recruitment of participants and data collection will take place in the households.

**II.iii. Sample size estimation**

The proposed surveillance study will be implemented in 36 subcenter area in the Solan District. The study will be conducted in collaboration with the Government of Himachal Pradesh. As per the suggestions from the Department of Health & Family Welfare of Himachal Pradesh, six sub-centre areas adjoining each of the five Community Health Centres and the Civil Hospital of Solan district will be chosen for the study. Each sub-centre area has a population of 3000 subjects of all ages. Assuming that the age group of >20 years constitutes about 50% of the total population, about 54,000 people will be enrolled in this study i.e.1500 from each of the 36 sub-centers.

Using STEPwise methodology [59] we estimated the sample size required to capture CMD risk factor prevalence. Utilizing risk factor prevalence estimates from previously published Indian studies and anticipating a response rate of 80 per cent (%) with a design effect factor of 1.5 (to account for cluster sampling), the sample size estimates were generated for males and females in five age strata (20-30, 30-40, 40-50, 50-60 and 60 and above. Table-1 presents the cumulative subtotals of subjects required to observe appreciably consistent prevalence approximations for each of the commonly-known risk factors. Since, the population that we plan to cover is more than the highest required sample size (37,816 people), it will permit to reliably estimate one or more of the CMD risk factors for each of the gender and age strata identified above.

Beyond this, we will conduct follow-up surveys to collect pilot data on incidence of risk factors, CMDs complications, and CMD-specific mortality. Consent will be taken during the initial recruitment for the cross-sectional survey and only those participants who provide consent to be followed up for four years will be enrolled into the study. However we anticipate an overall 15% loss-to-follow-up by the end of the cohort study especially due to high probability of migration of the young population (20-35 years) due to job opportunities or marriage (in case of females), and also because the study is community based.

***Table – 1 Sample size estimation***

| Risk factors | Level of Confidence | Margin of Error | Baseline levels of indicators | Design effect | Expected Response Rate | No. of age/sex Estimates | Sample size |
|---|---|---|---|---|---|---|---|
| Tobacco use | 1.96 | 0.02 | 0.3 | 1.5 | 0.8 | 10 | 37816 |
| Hypertension | 1.96 | 0.02 | 0.3 | 1.5 | 0.8 | 10 | **37816** |
| Diabetes | 1.96 | 0.02 | 0.04 | 1.5 | 0.8 | 10 | 6915 |

**Sub-Study:**

**With the support from NHLBI, blood samples will be collected in 4000 subjects using a multi-stage cluster random sampling technique considering equal proportions of males and females leading to a sample of 4000 participants.**

**Primary study design for original study is cross-sectional and a cohort study design will be used to follow-up the participants for four years subsequent to the cross-sectional study. Data collection for cross-section study stared in 2013 and is expected to be completed by May 2014.**

**The sub-study involves blood collection in a sub-sample of 4000 participants in this rural cohort at the baseline. For this, we plan to organize 100 blood sample collection camps in the clusters in six months to complete the proposed sub-study. Twelve phlebotomists will be recruited for blood sample collection from the camps and from households of selected participants. With this we will be able to complete the blood sample collection in 6 months."**

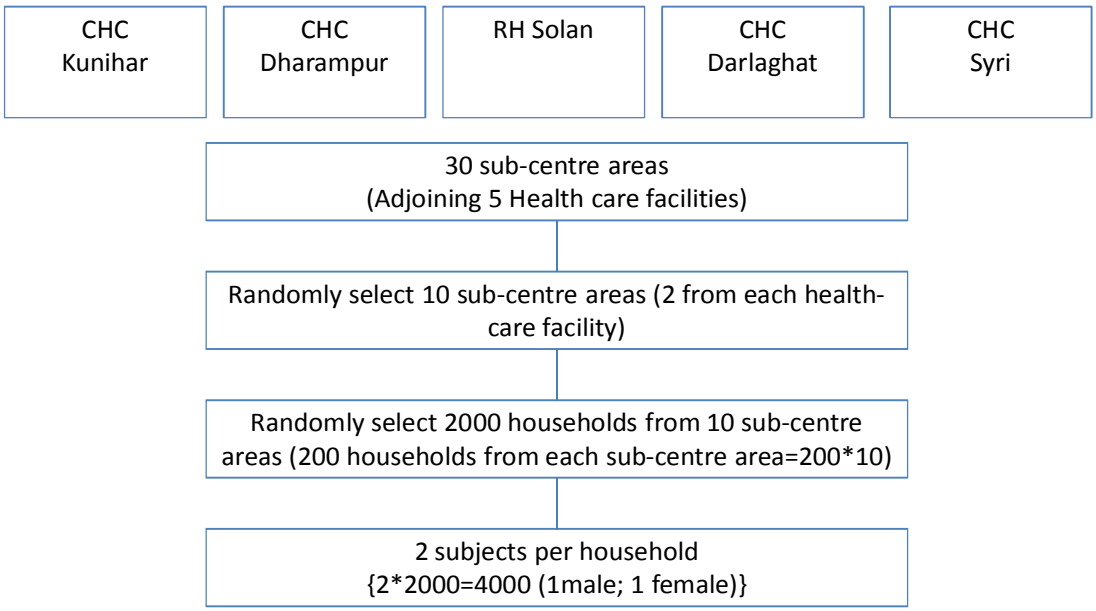
**Sampling methodology for sub-study:**

In Solan, 5 Government health care facilities (4 Community health centres and 1 regional hospital) were selected after recommendation from the health department, Solan. The six sub-centre areas adjoining each of the 5 healthcare facilities (i.e. 30 sub-centre areas) were selected based on proximity to the health facility.

The total sample size for the study is 4000 individuals. A multi-stage cluster random sampling technique will be used to capture a sample representative of the rural population. The 2 sub-centre areas will be selected randomly from each adjoining health care facility. From each sub-centre areas 200 households will be selected randomly. With informed consent, two subjects will be selected per household, one male and one female aged more than 20 years. The final sample for the study will be composed of equal proportions of males and females leading to a sample of 4000 participants (Figure 1).

**Figure 1: Diagrammatic representation:**

District Solan: 5 Health Care Facilities -




**II.v. Study tools**

Standardized sampling will enhance representativeness and reproducibility of results. Utilizing uniform tools and methods is a key component of this process and more easily replicable across multiple sites. We consulted validated questionnaires from the WHO Multinational MONItoring of trends and determinants in CArdiovascular disease (MONICA) study, WHO STEPwise Surveillance methodology, and existing questionnaires from regional and national surveys (accessible via partners at CDC), to construct a culturally appropriate and methodologically relevant questionnaire for India. Validated and new event (CVD or target organ damage) capturing tools was adapted to verify questionnaire-based follow-up survey incidence findings.

**II.vi Surveillance indicators**

A baseline cross-sectional survey of 54,000 participants in 2012-2013 will gather information encompassing broad categories such as: demographic and socio-economic characteristics of the population; presence of risk factors; previous or existing target organ damage (known nephropathy, angina, retinopathy, cataracts, peripheral vascular disease, previous stroke, previous therapeutic procedures such as amputation, revascularization procedure, peripheral endovascular procedure, dialysis, transplant, laser photocoagulation); quality of life, disability, health care utilization; quality,

- ***direct costs*** ('inputs' encompassing out-patient and in-patient care, pharmacotherapies, therapeutic procedures, and transportation to and from health care facilities in a given timeframe);
- ***indirect costs*** ('lost outputs' representing the value of economic productivity lost by society on account of temporary or permanent absence, disability, or premature mortality);
- ***health-related quality of life*** (including health utilities); and
- ***health outcomes*** (including incidence of new-onset risk factors, CVD events, morbidity, and mortality),

that may be used to model **societal burdens** of disease and potential avoidable mortality, disability, and costs with addition of proven interventions. Direct medical and non-medical costs will be ascertained from respondents through standardized questionnaires applied in other low- and middle-income countries. Data will also be collected from providers in different settings (private and government-funded clinics) to provide corroborated data for sensitivity analyses. Indirect costs will be estimated using a human capital approach which is based on data regarding absence from work and unit costs derived from national wage rates (for different occupation classes).

Lost production = total absence X wage rate of workers

Where possible, data regarding caregiver time and costs will be ascertained and included in analyses. The study will not collect data regarding foregone opportunities of children or other household members.

## II.viii. Qualitative exploration

### *II.viii.a. Background*

There is very little currently published regarding the knowledge, perceptions, attitudes, and care practices of people with cardio-metabolic risk factors and diseases in India. The surveillance study serves as a robust platform for investigating these qualitative aspects of cardio-metabolic diseases.

### *II.viii.b. Study questions*

1. - Identify valid indicators for assessment of the economic burden of CMD and their risk factors in different socioeconomic backgrounds and regions.
2. - Analyse the temporal trends and peculiarities of the socio-economic effects, knowledge, attitudes, perceptions, and practices of persons with risk factors (DM, HTN, Smokers)
3. - Knowledge, attitudes, perceptions, and practices of persons with cardiovascular (chronic stable angina, previous MI or UA, previous revascularization, PVD, previous stroke) and chronic kidney diseases

### III.ii. Data entry

A database application will be created using Microsoft access having a user friendly data entry screen in English. A data field specification list will be created along with a coding list for designing the database. The database will be programmed to have automated in-built checks for, logic, clinical reasonable such as ranges, absolute and relative values, context and structure. This will control the quality of data. The database will be assessed during the pilot study and necessary restructuring done before finalising it.

Data will be entered in the entry forms of the database centrally. Double data entry will be done for 25% of the forms to cross-check errors. There will be regular checks by site coordinator to minimise errors, missing values and outliers. Any errors found will be corrected by referring to the filled questionnaire or if required by a revisit to the participant. The data entry will be monitored and checked at CCDC. Final data cleaning and de-linking of participant identification information will be done at CCDC before conducting the analyses.

### III.iii. Data analysis

*(a) Quantitative Analysis*

Data analysis will be staggered to correspond to follow completion of each survey. All statistical analysis of quantitative data will be done using Statistical Analysis Software (SAS, version 9.1, SAS Institute, Cary, N.C)[60] or STATA (Statacorp, TX).[61]A probability of $p<0.05$ will be considered statistically significant for all tests. Assumptions of normally-distributed data will be assessed using plots and tests of normality. Non-normal variables will be transformed or categorized as required. All data will be presented before and after adjustment for confounding and testing for interactions.

Descriptive data analyses will be performed for all variables. Means, standard deviations, quartiles, and median levels of risk factors for each gender and age group will be reported. Comparisons across gender, age groups, and time periods will also be done using Chi-square and logistic regression for categorical variables, and t-tests and linear regressions for continuous variables. Evaluation of predictors of incidence and mortality will employ Cox's proportional hazards models. Response rates and percent retention will be evaluated by comparing the number of eligible individuals approached, number agreeing to participate, and successful follow-up over duration of surveillance studies.

*(b) Qualitative Data Analysis*

All interviews will be de-identified prior to analysis. The NVIVO version 10 program will be used to manipulate textual data for analysis. Analysis of the textual data will follow the grounded theory methodology whereby key themes are identified inductively from the textual data. These themes will then be compared using structured comparisons to identify specific issues.

| | Phase | | | |
|---|---|---|---|---|
| | **Design and Planning** | **Pilot Testing** | **Data Collection** | **Data Analysis** |
| | | to detect outliers | | |
| **Laboratory** | • Central procurement<br>• Develop internal and external quality assessment protocols and schedule of regularity | • Evaluate procedural fluidity<br>• Evaluate intra- -laboratory variability<br>• Interim analysis to detect outliers | • Internal quality checks and calibration<br>• Regular external validation – lyophilized samples from reference laboratory | • Assess intra-laboratory coefficients of variation |
| **Communication** | • Establish reporting structures<br>• Establish data transfer plans | • Assess agility of transfers | | |
| **Documentation** | • Develop checklists, logbooks<br>• Training in appropriate and legible documentation | • Assess recording legibility | | • Audit logbooks for response rates and field activity indicators |
| **Data Storage & Confidentiality** | • Establish data back-up and protection policies<br>• Training of all staff | • Assess accessibility, simplicity and flexibility of software | • Locked and password-protected data storage<br>• Active back-up | • De-identified datasets<br>• Limited access to personal identifiers |
| **Data Entry** | • Establish protocols, consistent data cleaning methods and verification systems | • Assess variability | • Interim analyses to identify duplicate entries<br>• Decision log to document issues | • Reporting on outliers<br>• Validity checks<br>• Track database errors |

**IRB = institutional review board; **SOP = standard operating procedures*

Validated questionnaires will be used to design the survey questionnaire and these along with the data collection forms will be peer-reviewed to ensure construct validity. Further the questionnaire will be pilot-tested in a small sample of population to ensure face validity. Rigorous training and familiarity with tools will minimize intra- and inter-observer variability. Key considerations throughout the process are consistency, strong leadership, communication, and adherence to clearly defined roles.

### V.ii. Anticipated challenges in quality assurance and suggested solutions

Concerns include encountering low response rates as well as loss to follow-up of participants. Suggested solutions are: (a) engaging communities to be sampled in advance and obtaining approval from local authorities; (b) leveraging our institutional reputations; (c) methodical application of training, regular surveyor motivation and encouraging positive, professional and respectful behavior towards respondents; (d) advance scheduling of visits that are convenient for respondents, and providing a list of subsequent visits; (e) storing and backing up contact details of all respondents surveyed and supplemental contact information (for relatives, employers) in an accessible format, while appealing to those surveyed to notify the network surveillance site office of any change of contact; and (f) identifying those at risk of mobility and customizing our approach accordingly. Our

investigators have extensive experience in recruiting and maintaining population cohorts (e.g., Industrial Surveillance Study, CARRS-Surveillance Study, New Delhi Birth Cohort Study, CUPS, and CURES).

## VI. Monitoring and evaluation

A Quality Monitoring and Evaluation (QME) sub-committee will be responsible for quality assurance of the study, will monitor all phases of the study and will conduct formative, process and outcome evaluation. The QME sub-committee will include the principal investigator, site coordinators and external evaluators. Progress of the study will be monitored through regular appraisal by the QME sub-committee.

### VI.i. Procedures for evaluating the process of the study

VI.i.1. Sampling*:*

a. - After the list of households from all the sub-centres are prepared, random checks will be done especially for areas that have been undergoing continuous development to ensure that all households are enlisted.

b. - Cross-check the household number generated with the number of the household in which participants were interviewed.

VI.i.2. Data collection**:**

a. - Initial shadow monitoring of all interviewers will be done for practical training and to resolve issues immediately. This will also help to identify weak personnel who may require intermittent supervision.

b. - As the study progresses, random checks for about 5-10% of the participants will be done every three months by site coordinators and project managers who will verify some of the answers in the filled questionnaires.

c. - There will be regular documentation of the response rates from participants especially for the follow-up of cohort to minimise loss to follow-up. The QME will also be responsible to audit these rates and other documented field activity indicators such that immediate corrective measure can be taken.

VI.i.3. Data entry:

a. - Project Manager will be responsible for checking all forms for completion or for any obvious errors before data entry.

b. - In-built checks in the data entry software – logic checks, context checks and ranges will be incorporated for outliers.

e. - Decision log will be used to document all issues related errors and queries (using excel sheets and emails)

f. - Monitoring data storage and confidentiality procedures: This will be done by the PIs and external evaluators at the CCDC after the complete collation of data and before using the data for analysis.

**VI.ii. Procedures for evaluating the outcome of the study**

1. - After the study is complete an independent evaluation will be done by the PIs and the external evaluators to ascertain if the aims and objectives of the study are fulfilled. This will be done through review of all the preceding evaluation processes, and also through review of the findings and results of the study.

## VII. Ethical considerations

Informed consent for interview, anthropometric measurements and blood collection will be taken from all individuals before enrolling them into the study. The study anticipates no major risk to participants except needle pricks for collection of blood sample during the follow-up and cross-sectional surveys. There could be rare instances of bleeding from the pricking site, however trained staff will minimise even the rarest of such possibility.

Supplemental Informed consent will be sought from the sub-study participants for blood sample collection and storage of left over blood for Genetic and metabolomic studies to identify genetic determinants of CMDs and their risk factors. Participation in this sub-study may involve some added risks or discomforts. These include: the risk of bleeding, bruising, and infection at the site of drawing blood. These risks will be minimized by having the blood drawn under sterile conditions by experienced personnel. Strict confidentiality of the information provided by the participants will be maintained and all possible source of identification of participants will be delinked before using the data for analysis.

## VIII. Timeline

The Surveillance Study will be conducted over a period of five years. The baseline cross-sectional survey will begin in 2012 with estimated completion time of twelve months. The participants will be then followed up as a cohort with biannual follow-up surveys for four subsequent years. Data analysis and reporting will take place after the collation of data at the end of the cross-sectional survey and thereafter at the end of annual follow-ups. Monitoring will be an ongoing process and the system of evaluation will be inbuilt into the study. The details of the timeline are provided in table-6.

***Table 6: Timeline for Surveillance Study***

| Surveillance Study | Timeline | |
|---|---|---|

**References**


1. - Kraushaar L, Kramer A. Are we losing the battle against cardiometabolic disease? The case for a paradigm shift in primary prevention. BMC Public Health. 2009;9(1):64.
2. - Mathers CD, Lopez AD, Murray CJL. The Burden of Disease and Mortality by Condition: Data, Methods, and Results for 2001. In: Lopez AD, Mathers CD, Ezzati M, Jamison DT, Murray CJL, eds. *Global Burden of Disease and Risk Factors,*. New York: Oxford University Press; 2006.
3. - International Diabetes Federation. The human, social & economic impact of diabetes. Available at: http://www.idf.org/home/index.cfm?node=41. Accessed February 2008.
4. - Economic Intelligence Unit. *The silent epidemic: An economic study of diabetes in developed and developing countries.* New York, London, Hong Kong: The Economist June 2007.
5. - Kempler P. Learning from large cardiovascular clinical trials: classical cardiovascular risk factors. *Diabetes research and clinical practice.* 2005;68 Suppl1:S43-47.
6. - Stamler J, Vaccaro O, Neaton JD, Wentworth D. Diabetes, other risk factors, and 12-yr cardiovascular mortality for men screened in the Multiple Risk Factor Intervention Trial. *Diabetes Care.* 1993;16(2):434-444.
7. - Ramachandran A, Snehalatha C, Latha E, Satyavani K, Vijay V. Clustering of cardiovascular risk factors in urban Asian Indians. *Diabetes care.* 1998;21(6):967-971.
8. - Pradeepa R, Mohan V. The changing scenario of the diabetes epidemic: implications for India. *Indian J Med Res.* 2002;116:121-132.
9. - Hughes LO, Raval U, Raftery EB. First myocardial infarctions in Asian and white men. *BMJ.* 1989;298(6684):1345-1350.
10. -McKeigue PM, Ferrie JE, Pierpoint T, Marmot MG. Association of early-onset coronary heart disease in South Asian men with glucose intolerance and hyperinsulinemia. *Circulation.* 1993;87(1):152-161.
11. -Ghaffar A, Reddy KS, Singhi M. Burden of non-communicable diseases in South Asia. *BMJ.* 2004;328(7443):807-810.
12. -Mohan V, Sandeep S, Deepa R, Shah B, Varghese C. Epidemiology of type 2 diabetes: Indian scenario. *Indian J Med Res.* 2007;125(3):217-230.
13. -Enas EA, Mehta J. Malignant coronary artery disease in young Asian Indians: thoughts on pathogenesis, prevention, and therapy. Coronary Artery Disease in Asian Indians (CADI) Study. *Clin Cardiol.* 1995;18(3):131-135.
14. -Radha V, Mohan V. Genetic predisposition to type 2 diabetes among Asian Indians. *Indian J Med Res.* 2007;125(3):259-274.
15. -Chambers JC, Elliott P, Zabaneh D, Zhang W, Li Y, Froguel P, Balding D, Scott J, Kooner JS. Common genetic variation near MC4R is associated with waist circumference and insulin resistance. *Nat Genet.* 2008;40(6):716-718.
16. -Yajnik CS. Early life origins of insulin resistance and type 2 diabetes in India and other Asian countries. *J Nutr.* 2004;134(1):205-210.
17. -Ramachandran A. Epidemiology of diabetes in India--three decades of research. *J Assoc Physicians India.* 2005;53:34-38.
18. -Lev-Ran A. Human obesity: an evolutionary approach to understanding our bulging waistline. *Diabetes Metab Res Rev.* 2001;17(5):347-362.
19. -Joshi P, Islam S, Pais P, Reddy S, Dorairaj P, Kazmi K, Pandey MR, Haque S, Mendis S, Rangarajan S, Yusuf S. Risk factors for early myocardial infarction in South Asians compared with individuals in other countries. *Jama.* 2007;297(3):286-294.
20. -Diaz VA, Mainous AG, 3rd, Baker R, Carnemolla M, Majeed A. How does ethnicity affect the association between obesity and diabetes? *Diabet Med.* 2007;24(11):1199-1204.
21. -McKeigue PM, Marmot MG, Syndercombe Court YD, Cottier DE, Rahman S, Riemersma RA. Diabetes, hyperinsulinaemia, and coronary risk factors in Bangladeshis in east London. *Br. Heart J.* 1988;60(5):390-396.
22. -McKeigue PM, Shah B, Marmot MG. Relation of central obesity and insulin resistance with high diabetes prevalence and cardiovascular risk in South Asians. *Lancet.* 1991;337(8738):382-386.

surveillance system for cardiovascular diseases in Indian industrial populations. *Bull World Health Organ.* 2006;84(6):461-469.
48. -Sethi R. Sample Registration System in India. September 02, 2008. Available at: http://www.searo.who.int/LinkFiles/2007_India1.pdf.
49. -Narayan KM, Benjamin E, Gregg EW, Norris SL, Engelgau MM. Diabetes translation research: where are we and where do we want to be? *Annals of internal medicine.* 2004;140(11):958-963.
50. -Goff DC, Jr., Brass L, Braun LT, Croft JB, Flesch JD, Fowkes FG, Hong Y, Howard V, Huston S, Jencks SF, Luepker R, Manolio T, O'Donnell C, Robertson RM, Rosamond W, Rumsfeld J, Sidney S, Zheng ZJ. Essential features of a surveillance system to support the prevention and management of heart disease and stroke: a scientific statement from the American Heart Association Councils on Epidemiology and Prevention, Stroke, and Cardiovascular Nursing and the Interdisciplinary Working Groups on Quality of Care and Outcomes Research and Atherosclerotic Peripheral Vascular Disease. *Circulation.* 2007;115(1):127-155.
51. -Morris AD, Boyle DIR, MacAlpine R, Emslie-Smith A, Jung RT, Newton RW, MacDonald TM. The diabetes audit and research in Tayside Scotland (darts) study: electronic record linkage to create a diabetes register. *Bmj.* 1997;315(7107):524-528.
52. -Morris AD, Boyle DI, McMahon AD, Greene SA, MacDonald TM, Newton RW. Adherence to insulin treatment, glycaemic control, and ketoacidosis in insulin-dependent diabetes mellitus. The DARTS/MEMO Collaboration. Diabetes Audit and Research in Tayside Scotland. Medicines Monitoring Unit. *Lancet.* 1997;350(9090):1505-1510.
53. -Evans JMM, Newton RW, Ruta DA, MacDonald TM, Stevenson RJ, Morris AD. Frequency of blood glucose monitoring in relation to glycaemic control: observational study with diabetes database. *Bmj.* 1999;319(7202):83-86.
54. -Evans JM, McNaughton D, Donnan PT, MacDonald TM. Pharmacoepidemiological research at the Medicines Monitoring Unit, Scotland: data protection and confidentiality. *Pharmacoepidemiol Drug Saf.* 2001;10(7):669-673.
55. -Evans JM, MacDonald TM, Leese GP, Ruta DA, Morris AD. Impact of type 1 and type 2 diabetes on patterns and costs of drug prescribing: a population-based study. *Diabetes Care.* 2000;23(6):770-774.
56. -Joshy G, Simmons D. Diabetes information systems: a rapidly emerging support for diabetes surveillance and care. *Diabetes Technol Ther.* 2006;8(5):587-597.
57. Clifford GD, Blaya JA, Hall-Clifford R, Fraser HS. Medical information systems: a foundation for healthcare technologies in developing countries. *Biomed Eng Online.* 2008;7:18.
58. Rizzo L, Brick JM, Park I. A minimally intrusive method for sampling persons in Random Digit Dial surveys. Public Opinion Quarterly. 2004;68(2):267-74.
59. - World Health Organization. STEPwise approach to surveillance (STEPS). Available at: http://www.who.int/chp/steps/manual/en/index.html. Accessed September 28, 2008.
60. SAS I. SAS/STAT Users Guide Version 6. Cary, NC: SAS Institute; 1990.
61. StataCorp LP. STATA Data Analysis and Statistical Software. Available at: http://www.stata.com/.
62. Neaton JD, Duchene AG, Svendsen KH, Wentworth D. An examination of the efficiency of some quality assurance methods commonly employed in clinical trials. Statistics in Medicine. 1990;9(1-2):115-24.
63. Day BS, Fayers BP, Harvey BD. Double Data Entry: What Value, What Price? Controlled Clinical Trials. 1998;19(1):15-24.