



# Strong Heart Study Newsletter

Investigating Cardiovascular Disease in American Indians

Volume 24, Issue 1 Spring 2014

## The Strong Heart Study at 25 Years

The Strong Heart Study (SHS) had its 25th anniversary in 2013. This issue of the Newsletter is a brief overview of the study, providing the reader with some of its significant accomplishments and outlining work to be carried out in Phase 6 of the study.

The SHS began with a 1988 grant by the National Heart, Lung, and Blood Institute (NHLBI). The purpose of the SHS is to study cardiovascular diseases (CVD) and their risk factors among 13 American Indian tribal groups residing in North and South Dakota, southwest Oklahoma, and Arizona. A total of 4,549 tribal members ages 45-74 years were in the original group (cohort) studied.

The following questions were addressed: 1) Is CVD an important public health problem in Indian communities? 2) What is the occurrence of CVD risk factors and how do they vary? 3) How does CVD among Indians compare to CVD among non-Indian communities? 4) Can these types of scientific studies involving multiple research sites be successfully conducted in Indian country?

The following objectives were established:

- 1) Measurements of rates of CVD;
- 2) Measurements of CVD risk factors and their rates;
- 3) Determination of the effect of diabetes on CVD;
- 4) Follow-up of participants to study trends in CVD and its risk factors;

- 5) A survey of the group for all causes of morbidity and mortality.

### *PHASE 1 (1988 – 1991)*

The initial studies consisted of participants' medical history; physical exams; an electrocardiogram; a questionnaire with the usual demographic data; and a variety of laboratory examinations. Blood, urine and DNA samples were obtained and stored for further study.

All causes of mortality were examined through review of clinical records and death certificates. Medical records were reviewed for all causes of mortality and CVD morbidity. Clinical records of all possible CVD deaths were reviewed for any associated risk factors.

Participants were contacted annually in order to determine if any had experienced intervening CVD events.

### *PHASE 2 (1992 - 1995)*

Most of the examinations conducted in Phase 1 were repeated with the addition of echograms (ultrasounds) of the heart and pulmonary function testing to detect emphysema and/or asthma. Clinical records continued to be surveyed for causes of death and risk of CVD.

### *PHASE 3 (1996 - 2000)*

In addition to continued surveillance, or review, of clinical records, certain examinations were added: carotid ultrasound to look for plaques in the neck arteries; testing for how pressure waves travel through the arteries; measurement of carbon monoxide in



exhaled air; and a pilot program to study the occurrence of CVD in family groups was conducted.

#### ***PHASE 4 (2000 - 2005)***

Two important studies were added. Based upon the pilot study in Phase 3, a second study was added: the Strong Heart Family Study (SHFS). The SHFS consists of 3,838 participants, ages 15 years and older from large families. Examinations were similar to those of the original group. The SHFS permitted searches for genes possibly affecting CVD, diabetes and their respective risk factors. The other addition was the Stop Atherosclerosis in Native Diabetics Study (SANDS), a clinical trial, which examined whether stricter control of blood pressure and cholesterol in individuals with diabetes would help prevent CVD. The results showed there was improvement in atherosclerosis and the functioning of the heart.

#### ***PHASE 5 (2005 - 2013)***

We continued to examine for CVD and other causes of death. We also conducted a re-examination of the family group.

Another ancillary study, the Strong Heart Stroke Study (SHSS) was instituted. It utilized brain scanning to further define when certain changes in the brain could represent a “silent” stroke, a previously relatively unstudied condition among Indian people.

The period between 2010 and 2013 was taken up by continued applications for funding to carry the study into Phase 6. During this time, we continued to examine for CVD events and were able to carry out a number of ancillary studies by utilizing SHS stored samples and data.

#### ***SOME IMPORTANT FINDINGS AND ADVANCES***

Early results of the SHS disclosed several important findings:

1. Rates of coronary heart disease (CHD) higher than those for other US populations of the same age;
2. Most of the CVD events occurred in individuals who had diabetes (diabetes was found to affect one-half the original study population);
3. Even though levels of LDL, or “bad” cholesterol, are generally lower for the SHS participants than for the general US population, LDL remains a strong predictor of CVD for Indian people;
4. Development of an equation that permits better estimation of CHD risk, specifically for Indians;
5. The importance of small amounts of protein (albumin) in the urine (a measure of damage to the kidneys) as a marker for later CVD;
6. Echograms of the heart of younger Indians disclosed abnormal changes in the hearts and blood vessels, evidence of early CVD;
7. Reduced physical activity and increased intake of processed meats are associated with more diabetes;
8. Mental and emotional depression are linked to degree of glucose control in diabetic patients;
9. Genetic analyses identified changes on chromosome 12 that affect heart size and on chromosome 9 that affect heart rate;



The Strong Heart Study team from all centers in South Dakota in 2003.

The SHS has published more than 300 medical and scientific reports. It has supported more than 35 young American Indian investigators and clinicians. It has established algorithms and guidelines for use by Indian Health Service (IHS) and other physicians.

### ***ANCILLARY (ADDITIONAL) STUDIES***

SHS data and stored specimens have permitted a great number of ancillary studies, all related to CVD and its risk factors among American Indians, multiplying the number of studies that can be done.

Some of the ancillary studies include:

- 1) Sleep Heart Health Study;
- 2) Stop Atherosclerosis in Native Diabetics Study (SANDS);
- 3) Strong Heart Stroke Study (SHSS);
- 4) Studies relating inflammation to CVD;
- 5) Investigation of environmental arsenic exposure and CVD risk;
- 6) Detailed mapping of genetic changes on chromosome 17 that affect blood pressure;
- 7) Many genetic analyses identifying changes related to diabetes, metabolic syndrome, obesity and kidney function;
- 8) The level of sex hormones and their relation to CVD;
- 9) Demonstration that genetic risk factors for CVD are present in the SHS overall at the same level as for the general US population;
- 10) Examination of the relationship of telomeres, which are found at the end of chromosomes, to both aging and type 2 diabetes;
- 11) Genetic changes in the Oklahoma study population may be related to liver function and a protective factor against heart disease;
- 12) Genetic studies and educational efforts to more fully understand end stage kidney disease;

### ***PHASE 6 (2014 - )***

We will continue to use stored specimens and data for various ancillary and sub-studies, including genetic investigations. Continued surveillance also remains a priority. The same rules of privacy will continue, including removal of all identifying participant data. We will continue our special interface and sharing of information with the respective tribes and participants. While budget restrictions prevent us from pursuing certain goals, we will broaden the scope of the study to include other important illnesses, with a focus on cancer, the second leading cause of death of American Indians. Examinations of participants will not be possible because of budget reductions. However, a questionnaire will be administered that will focus on other serious causes of illness and mortality. We will continue to survey morbidity and mortality, including cancer and continue studies of possible genetic risk factors. We will continue to store specimens and maintain the extensive data base and respond to requests for uses of these for appropriate ancillary studies.

### ***RELATIONSHIP OF SHS WITH PARTICIPANTS AND TRIBES***

A mark of unique SHS success is the continuing relationship with its participants and tribal officials. This is reflected in the very high rates of retention in the study. This relationship is maintained by the distribution of many reports compiled specifically for community use and by regularly meeting with tribal officials and health boards. This success is largely the result of the insistence by the SHS investigators that they operate in partnership with the tribes and participants. The SHS strictly adheres to Department of Health and Human Services and IHS rules regarding the privacy and confidentiality of research participants.

To further protect the participants, tribes and IHS, we require tribal and community approvals for all scientific publications and modifications related to the study.

Participant/Tribe concerns and privacy are also governed by several university, IHS, NHLBI and other institutional review boards (IRBs) who oversee the study.

STRONG HEART STUDY COORDINATING CENTER  
University of Oklahoma Health Sciences Center  
Center for American Indian Health Research  
College of Public Health  
P.O. Box 26901  
Oklahoma City, OK 73126-0901

Non-Profit Organization  
U.S. Postage  
PAID  
Oklahoma City, Oklahoma  
Permit No. 220

The data and samples are tightly guarded and are not released without permission from the communities. When a serious condition is found during the examination of a participant, the results are reported to the participant and assistance is provided to obtain proper medical attention. This has been very helpful in preventing further heart disease for a number of participants. The individual is only identifiable to local SHS staff for the purpose of follow up and isn't identifiable to other investigators. All information is entered into the SHS database only after removal of all personal identity information.

### ***CHALLENGES***

Since 2004, the SHS has had many discussions with NHLBI regarding the effect of the NIH/NHLBI requirement that raw data resulting from certain studies (including SHS) must be made available to all qualified investigators who wish to do analyses. Under the doctrine of tribal sovereignty and the resulting government to government relationships, and in recognition that perspectives held by Indian people must be respected, the SHS continues to insist that this

matter can only be resolved between the NIH/NHLBI and the respective tribes.

The SHS insists that it is obligated to respect the decisions of the tribes in regard to any questions related to the ultimate disposition of specimens and data.

In addition to the important advances in medical knowledge made by the SHS, the investigators value the close personal relationships that have been maintained over the years, especially with the participants and the many local Native field workers. The SHS has enjoyed excellent support from the IHS, particularly at the local level. Provision of space, availability of clinical records, and other support, without which the study could not be conducted, are greatly appreciated.

We look forward to continued collaborations with the tribes and participants to whom this issue of the Newsletter is dedicated. There is every reason to expect that the partnerships will continue to provide important information that should be useful to the community.

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