

## Cardiovascular Epidemiology: The Legacy of Sound National and International Studies

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The expression “Cardiovascular Epidemiology” has been widely used in observational studies that assess risk factors for cardiovascular disease. However, it includes research in biology, behavior, treatment and prevention of cardiovascular disease. In addition to exploring the relationship between risks of health conditions and states of diseases that can be hardly tested in experimental studies, epidemiology provides methodological arsenal to launch cause-effect connections, establishing the basis for cardiovascular prevention.

Large cohort studies have provided information on the etiology and prevention of cardiovascular disease that built a great part of the current medical knowledge. The well-known Framingham Heart Study is among the pioneer cohort studies<sup>1</sup>. This study was conducted in Framingham, a 28,000 inhabitant’s town located 21 miles west of Boston. The study enrolled 6,000 medium class Americans, 30 to 59 years old, mostly white, who were followed for 20 years. The study focused on risk factors for coronary heart and cardiovascular disease. It was exemplary planned, conducted and analyzed, establishing the basis of much that we know about causation of cardiovascular disease. Countless studies were inspired by the Framingham experience, expanding the epidemiological framework of several risk factors and diseases. The Atherosclerosis Risk in Communities (ARIC) study investigated the etiology of atherosclerosis and its clinical outcomes, and variation in cardiovascular risk factors, medical care, and disease by race, sex, place, and time. In a different way of the Framingham study, this cohort was conducted in three ethnically mixed communities - Forsyth County, North Carolina, and suburbs of Minneapolis, Minnesota, and Washington County, Maryland - and in one black community – in Jackson, Mississippi - enrolling 4,000 adults, aged 45-64 years, from each community, who were examined twice, three years

apart<sup>2</sup>. An extensive laboratory with biochemistry assessment and ultrasound scanning of carotid and popliteal arteries were innovative methods investigated in this study<sup>3</sup>.

The Nurses’ Health Study (NHS)<sup>4</sup> and the Health Professionals Follow-up Study (HPFS), led by Harvard University, Boston, Massachusetts, started addressing restricted questions among professional groups of women and men. The NHS was planned to investigate the long-term consequences of the use of oral contraceptives among a highly cooperative motivated group of women, the American registered nurses, aged 30 to 55, in 1976, who lived in the 11 most populous states of the US - California, Connecticut, Florida, Maryland, Massachusetts, Michigan, New Jersey, New York, Ohio, Pennsylvania, and Texas. Approximately 122,000 nurses, out of the 170,000 mailed, responded the baseline questionnaire, and every two years members received a follow-up questionnaire with questions about diseases and health-related conditions including smoking, hormone use and menopausal status. In subsequent follow-up inquiries, diet and nutrition data were collected. The subsequent Nurses’ Health Study II and III investigated younger nurses and expanded the investigation to other research questions<sup>5</sup>.

The Health Professionals Follow-up Study enrolled 51,529 men – mostly dentists and veterinarians, but also pharmacists, optometrists, osteopath physicians, and podiatrists, including a small sample of African- and Asian-Americans. The aim was to investigate men’s health associated to nutritional factors over the incidence of cancer, heart disease, and other vascular diseases. The data collection was carried out using self-answered questionnaires with questions about diseases and alcohol consumption, health-related topics like smoking, physical activity, and medications taken every two years, and dietary information each four-year intervals<sup>6</sup>. The studies commented above gave origin to more than 7,700 papers and countless citations, which are the foundation for the current cardiovascular disease knowledge.

These large cohort studies are a few examples of very expensive studies, which demanded long follow-up periods, supported by the American government agencies. In Brazil, pioneer studies were fully funded by international agencies, as the Pelotas birth cohort study, which enrolled more than 5,000 newborns and their families at about 30 years ago. It has shown the development of cardiovascular risk factors linked to perinatal outcomes<sup>7,8</sup>. The Brazilian government has recently started to fund large epidemiologic and clinical studies. Beside to answering relevant questions to the Brazilian population, these studies will contribute for the universal knowledge of

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cardiovascular disease causation, prevention and treatment. The ELSA study (*Estudo Longitudinal da Saude do Adulto*) is an example of a large cohort study being conducted in the adult Brazilian population<sup>9</sup>. It is investigating the risks and prognosis of diabetes and cardiovascular disease in a cohort of more 15,000 employees of universities and affiliated hospitals. Large clinical trials have been sponsored as well by Brazilian agencies, such as the PREVER Prevention<sup>10</sup> and Treatment<sup>11</sup> trials, and the Stem Cell Therapy Trials for the management of cardiac conditions<sup>12,13</sup>. Other clinical studies as the ReHot, which is investigating the prevalence and treatment of resistant hypertension, are on the way currently.

These studies are evidences of the experience of Brazilian investigators, who could plan and conduct such kind of studies. The complementary strengths of observational studies and randomized clinical trials expands the knowledge of cardiovascular disease determinants, prevention, and treatment. Besides the scientific benefits, we are breaking down barriers, improving skills in coordination and conduction of large national studies, fomenting junior investigators, and mentoring clinical and research fellows. The legacy of these sound studies will certainly change the way we understand and practice cardiology.

In the I Symposium of Cardiovascular Epidemiology, recently carried out in Porto Alegre, Professors, physicians, post-doctoral fellows, graduate and medical students experienced integration between the Brazilian and the international cardiovascular epidemiology research.

Brazilian and international speakers, including Paul K. Whelton (ALLHAT PI)<sup>14</sup>, Peter Libby (Inflammation investigator, Chief of Cardiology Division of Brigham Women' Hospital, Harvard University)<sup>15</sup>, Thomas Lee (Health Policy and Management investigator, Harvard University)<sup>16</sup>, and Lu Chi (Harvard University)<sup>17</sup>, presented their main ongoing projects and several sessions of state of art updating the knowledge on cardiovascular epidemiology. This issue of the *Arquivos Brasileiros de Cardiologia* has a supplement with 72 abstracts presented at the Symposium, examples of the products of clinical and epidemiological research in our country. Three of them were awarded: two randomized clinical trials and a cost-effectiveness analysis study (see the stars in the abstracts). The Symposium was also conducted in honor of Professor Jorge Pinto Ribeiro legacy. Professor Jorge left an enormous contribution to science and a legion of academic orphans, as can be seen by some of his last articles published<sup>18-28</sup>. His sound work and competence helped to improve research and cardiology practice, not only locally, but nationwide. Hospital de Clínicas de Porto Alegre (HCPA) will honor him naming the Clinical Research Building on Professor Jorge Pinto Ribeiro behalf. In addition, three prizes were instituted on his name: for leading scientists, who made major academic contributions, an outstanding young investigator, and a policy maker, who helped the HCPA to achieve its aims in excellence of health assistance and quality of care. We hope that the *Arquivo's* readers enjoy the high quality of the abstracts presented at the Symposium.

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