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# Setting up the Longitudinal Study for Adult Health (ELSA-Brasil)

Baseline data collection of the Brazilian Longitudinal Study for Adult Health (ELSA-Brasil) was complete by December 2010. A cohort of 15,105 subjects has been followed up on incident events at six study sites for three years. The ELSA-Brasil is remarkable for its large sample size and wide variety of data collected to investigate biological and social determinants of cardiovascular diseases and diabetes mellitus in adults in Brazil. A group of Brazilian experts in chronic noncommunicable disease research started planning this study project in 2004. It was launched at a meeting on August 20 to 21, 2004 held at the Universidade de São Paulo University Hospital (HU-USP) in São Paulo, Brazil.

## THE BACKGROUND

In Brazil, researchers of cardiovascular disease epidemiology routinely engaged in collaborative work on specific projects and knowledge exchange at conferences and seminars. In São Paulo, more specifically at the HU-USP, a follow-up study was being developed with a sample of university workers who had undergone work-related medical examinations in 1998.<sup>21</sup> This study was initially supported by the São Paulo Research Foundation (FAPESP) in 2002, but it was then canceled due to high import costs. At the same time researchers from the Universidade do Estado do Rio de Janeiro and Fundação Oswaldo Cruz (Fiocruz), both in Rio de Janeiro, launched a more structured research project, the Pró-Saúde Study.<sup>9</sup>

The São Paulo project focused on risk factors and subclinical cardiovascular disease indicators while the Pró-Saúde Study investigated social aspects involved in the development of these diseases. Since there was significant overlapping of clinical endpoints, the two groups proposed to develop common questionnaires and assessments including anthropometric assessment and blood pressure measurements. During their first interaction they came up with the idea of designing a more comprehensive study project that would involve other research groups with extensive experience in cohort studies in Brazil including the Rio Grande do Sul (Atherosclerotic Risk in Communities Study),<sup>19</sup> the Minas Gerais (Bambuí Project),<sup>4</sup> and the Espírito Santo (The WHO MONICA project) groups.<sup>7</sup> In order to scale the project up and involve as many research centers with relevant experience those groups working on the epidemiology of cardiovascular diseases or diabetes with major work published were invited to join in. The Universidade Federal da Bahia Collective Health Institute (ISC-UFBA) research group was the first to embrace the project and other groups joined the project with the purpose of further explore this topic over that year of 2004. The study was then funded by the HU-USP Medical Research Division.

## THE PROPOSED PROJECT

The project's background document highlighted key aspects of science and technology policies applied to the epidemiology of chronic noncommunicable diseases including the relative exhaustion of cross-sectional designs, a pressing

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need for long-term as well as multicenter, multidisciplinary studies to explore the complex health-chronic disease phenomenon against a social context of great cultural and socioeconomic disparities in Brazil.

Three major ‘assets’ were identified: extensive experience of Brazilian researchers in conducting and/or analyzing longitudinal studies of chronic diseases in Brazil and abroad; collaboration with major research centers including Harvard University (Nurses’ Health Study);<sup>a</sup> collaborative work in cohort studies such as the Atherosclerotic Risk in Communities Study,<sup>b</sup> The Whitehall Study,<sup>c</sup> The World Health Organization MONICA Project,<sup>d</sup> and The Framingham Heart Study;<sup>e</sup> and a need for conducting a study with robust design and methodology approaches and in-depth analysis.

Over two years the group of researchers met periodically to develop specific study objectives, design sampling methods, select major exposures and outcomes, structure the study’s organization, create a database and discuss ethical issues and communication approaches. Supported by the Brazilian Ministry of Health Department of Science and Technology (Decit/MS), a study protocol was fully developed and a permanent, fixed population of workers was selected to make it easier to follow-up subjects over time as the population drawn from the very labor force of research centers involved in the study. All medical assessments and measurements would be performed locally at each study site except for more complex tests such as electrocardiogram and retinography that would be performed centrally. A central laboratory was established for conducting all biochemical tests and a biobank was set up as a central repository to store all biological samples. Finally, a Data Center was implemented to develop and manage the study database. Detailed information about the study development can be found in the articles published in this supplement.

## THE PROPOSED PROJECT AND FINANCIAL SUPPORT

The project’s background document was submitted to several stakeholders at Brazilian research funding agencies. The first positive response came from Professor Reinaldo Guimarães who was then the director of the Decit/MS. He has played a leading role in promoting major changes in health research financing.<sup>14</sup> A month later the study proponents met with representatives from the Decit, the Funding Authority for Studies and Projects (FINEP) and the National Council for Scientific and Technological Development (CNPq) in São Paulo to present and discuss the proposed project. They received full support and they were granted funds for meetings of working groups held 2005 and hiring of a Ministry of Health consultant for technical supervision. These resources (seed money) were crucial for developing a solid proposal that would be scientifically and operationally feasible in Brazil.

The work on the project’s organization structure continued at a fast pace. A new meeting was held in November 2004 where it was named the “ELSA Project.” Almost all exposure and outcome variables to be investigated in the

<sup>a</sup> The Nurses’ Health Study. Boston: Channing Laboratory; s.d. [cited 2013 Apr 28]. Available from: <http://www.channing.harvard.edu/nhs/>

<sup>b</sup> National Heart, Lung and Blood Institute; University of North Carolina at Chapel Hill. Atherosclerosis Risk in Communities Study. Chapel Hill; s.d.[cited 2013 Apr 28]. Available from: <http://www2.csc.unc.edu/aric/>

<sup>c</sup> University College London, Research Department of Epidemiology and Public Health. The Whitehall II Study (Stress and Health Study). London; s.d. [cited 2013 Apr 28]. Available from: <http://www.ucl.ac.uk/whitehallii>

<sup>d</sup> World Health Organization; MONICA Collaborating Centres. The WHO MONICA Project. [cited 2013 Apr 28]. Available from: <http://www.ktl.fi/monica/>

<sup>e</sup> National Heart, Lung and Blood Institute; Boston University. Framingham Heart Study. Framingham; s.d.[cited 2013 Apr 28]. Available from: <http://www.framinghamheartstudy.org/>

ELSA-Brasil were selected but the number of study sites (five to eight) and the sample size (15,000 to 19,000 subjects) had yet to be determined. During this meeting it was established a goal that proved unfeasible from an administrative perspective: to expand the project to other research centers that were not involved in the ELSA-1 and create the ELSA-2.

In May 2005, the appointed Ministry of Health consultant, Professor Moyses Szklo from Johns Hopkins School of Public Health, met with the project's researchers. He made a significant contribution to the project given his extensive experience in coordinating three major U.S. cohort studies, particularly the Atherosclerosis Risk in Communities Study and the Multi-Ethnic Study of Atherosclerosis. These studies served as a model for developing the ELSA-Brasil research protocols and guided the selection of many exposures and subclinical atherosclerosis indicators and the creation of research committees especially the Publications and Presentations Committee. Prof. Szklo's involvement made it possible for the research group to have full access to these studies' research protocols.

On October 14, 2005 the MCT/MS/Decit/FINEP Public Call 02/2005 was opened for selection of proposals for a national research consortium of centers. The selected centers would be involved in the development of the Multicenter Longitudinal Study in Cardiovascular Diseases and Diabetes with support from the Decit and the Health Care Fund totaling US\$ 10.5 million. In December 2005 the winning consortium was announced. This consortium comprised six higher education and research institutions and centers from six different states in Northeast (Universidade Federal da Bahia – UFBA), Southeast (Fundação Oswaldo Cruz – Fiocruz; Universidade de São Paulo – USP; Universidade Federal de Minas Gerais; and Universidade do Espírito Santo) and South Brazil (Universidade Federal do Rio Grande do Sul). They submitted an operational plan and budget for approval of the funding agencies and the initial funding was provided over the first half of 2006 following an agreement signed with the supporting foundations affiliated to the six centers involved in the study.

### THE ELSA-BRASIL ORGANIZATION STRUCTURE

The project's structure comprises six study sites, five reading centers,<sup>6</sup> a central laboratory,<sup>13</sup> a biobank<sup>17</sup> and a data center.<sup>12</sup> The project is managed collectively and its governing body is the Research Steering Committee aided by assisting committees and an External Advisory Committee. The study activities take place at local site facilities in especially designated areas. All six sites have conducted subject recruitment,<sup>2</sup> interviews,<sup>10</sup> medical assessments,<sup>6,15</sup> and biological sample collection, analysis, storage and transport.<sup>13,17</sup> They also follow up subjects according to the guidelines set forth by the Clinical Outcome Committee (COC).<sup>5</sup> The reading centers are run at specific sites (Rio Grande do Sul, São Paulo, Minas Gerais and Espírito Santo) with local technical and staff capabilities. The central laboratory<sup>13</sup> and biobank<sup>17</sup> are hosted at the São Paulo site and the Data Center at the Rio Grande do Sul site.<sup>12</sup>

The study sites developed standard procedures for performing complex assessment as well as provided training and certification of their staff in testing and result reading.<sup>6,10,15</sup> The results of medical assessments and measurements including electrocardiograms,<sup>18</sup> echocardiography, retinography, pulse wave velocity, and abdominal and vascular ultrasound are coded and data is transferred to the ELSA-Brasil reading centers. There are seven biorepositories to ensure safe storage of biological samples (urine, serum, plasma and DNA) collected from subjects. Six of them store samples collected locally in freezers (-80°C) and a central biorepository in the Sao Paulo site stores biological samples in liquid nitrogen tanks (-192°C).<sup>17</sup>

Other international consultants have collaborated with the implementation of the Data Center and reading centers and the design of approaches for identification and categorization of incident outcomes of interest.

## **THE RESEARCH STEERING COMMITTEE AND ASSISTING COMMITTEES**

The ELSA Research Steering Committee (ERSC) is composed of six research managers from each site, the Data Center manager, a Decit representative, a FINEP representative and a technical consultant appointed by the Decit. The ERSC appointed representatives from all sites to form assisting committees. Their role is to discuss, propose and evaluate actions to be implemented in the project. The Sampling and Monitoring Committee established guidelines for sample selection and subject recruitment as well as for the characterization of nonrespondents among the eligible population.<sup>2</sup> The ELSA Exposures Committee (EEC) developed all questionnaires and procedures for their administration.<sup>10</sup> The Medical Assessment Committee set standard procedures for anthropometric and blood pressure measurements and electrocardiogram, among others, and set the parameters for capture and transmission of functional and imaging data.<sup>14,15</sup> The Clinical Outcome Committee set forth strategies and actions for subject follow-up and identification, ascertainment and categorization of incident events of interest.<sup>5</sup> The Sampling and Laboratory Analysis Committee developed procedures for laboratory analyses and quality control of all tests and has supervised sample collection, analysis and transport locally at site laboratories. It also established storage procedures to ensure quality of frozen samples including training of technical staff in result monitoring.<sup>13,17</sup> The Quality Assurance and Quality Control Committee established quality assurance and control procedures and encouraged with the support of site supervisors reliability and validity studies of variables being investigated.<sup>20</sup> The Ethics, Recruitment and Social Communication Committee set out guidelines for subject contact, communication with institutional review committees, and data confidentiality in occupational cohorts to guarantee subjects' rights and data reliability.<sup>3</sup> The Publications and Presentations Committee's role is to review proposed publications and presentations of the study results as well as proposed dissertations and theses.<sup>8</sup> The Data Center has supported the study planning and development including sampling, data collection, processing and analysis, training and certification/recertification of interviewers and evaluators, quality control, pre-testing and pilot testing. It also provides operations management. However, the ERSC is the one that makes the final decisions about sensitive issues, key topics and disagreements among committees to ensure the project's quality and longevity.

## **THE IMPACT OF ELSA-BRASIL**

The ELSA-Brasil project was launched in 2004 and from August 2012 it has been running the second round of subject assessments. The study data generated will provide valuable input for the formulation of the National Public Health System policies by describing the status of the main cardiovascular risk factors such as hypertension, diabetes and dyslipidemia and their prevalence, and characterizing subject awareness of their conditions and risk factor control and treatment.<sup>9</sup> Besides input to health managers, the ELSA-Brasil findings may provide extremely valuable information to medical specialists by showing the distribution of several tests performed in Brazil including carotid intima-media thickness and pulse wave velocity that are based on normal values from international populations. In addition, the investigation of social variables such as ethnicity may provide a more consistent ground for social inclusion policies. The scientific community has adopted several technologies used in the study such as cryobiology systems.

But the ELSA-Brasil impact goes beyond gains arising from findings of data analyses. The project's experiences have tear down the myth that long-term longitudinal studies on chronic diseases are not feasible in Brazil. They also have dispelled the anathema that the Ministry of Health should not supervise scientific projects. The Decit's guidance has been key not only to the ELSA-Brasil but to other studies because it has allowed to overcoming the traditional practice of conducting large cooperative research studies exclusively grounded in science. Possibly the most invaluable contribution of the ELSA-Brasil is to have established cooperation networks with a shared goal allowing people with different expertise to work harmoniously and further adding value to the study at each site. Each study site has shared its past experience and knowledge among other researchers while at the same time it has benefited from this very exchange. This quality leap was only possible with close cooperation among them.

The future of ELSA-Brasil is to continue following up subjects and performing periodic waves of reassessments to collect data on the incidence of cardiovascular diseases such as coronary and cerebrovascular disease, as well as is to provide major input into the emerging determinants of chronic diseases including renal failure, heart failure and disabilities such as blindness and dementia.<sup>1</sup>

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