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**‘MAJOR AWARDS TO CENTRES OF EXCELLENCE IN LATIN AMERICA’
Application for a Programme Grant
under the Health Consequences of Population Change Programme**

Q1 Applicants	Principal Applicant	Co-applicant (1)
Surname		
Forenames	s	
Title		
Position		

	Co-applicant (2)	Co-applicant (3)	Co-applicant (4)
Surname			
Forenames	.		
Title			
Position			

Q2 Name and address of employing institution:

Q3 Period for which support is sought (state in months):

Q4 Proposed start date (dd/mm/yy):

Q5 Title of programme (no more than 220 characters):

Costa Rican Healthy Aging: longitudinal study of life course changes in survival, health, and living arrangements and their socioeconomic determinants.

Principal applicant:

Luis Rosero-Bixby

Title of project:

Costa Rican Healthy Aging: longitudinal study of life course changes in survival, health, and living arrangements and their socioeconomic determinants.

UNDERTAKINGS

(i) In signing the application form where shown below, and in consideration of the receipt of this application by the Trust, all **applicants** (principal applicant, coapplicant, sponsors) UNDERTAKE that the information provided in the application form and otherwise in connection with this application is to the best of their knowledge and belief accurate and complete and that, in relation to any Award of Grant resulting from the application, they will:

1. Take all reasonable actions to ensure that the Trust's contribution to the funding of the research is suitably acknowledged.
2. Ensure that all research papers (whether based wholly or partly upon the research to be funded by the grant) are forwarded to the Trust upon publication.
3. Comply as Trust-funded researchers with the Trust's principles and policies on relationships between Trust-funded researchers and commercial entities as set out in Annex A to the Trust's grant conditions.
4. Consult with the Trust's subsidiary, Catalyst BioMedica Limited, prior to entering into an arrangement with any enterprise that will provide for the exploitation of any results arising from any activity funded under a Trust award.
5. Promptly inform the Trust of any material changes during the period of the Grant to any of the details provided in this application.

I have read the conditions under which grants are awarded and the undertakings detailed above and, if a grant is made, I agree to abide by them. I shall be actively engaged in the day to day control of the project.

Signature of Applicant

Date:

Signature of Coapplicant (1)

Date:

Signature of Coapplicant (2)

Date:

Signature of Coapplicant (3)

Date:

Signature of Coapplicant (4)

Date:

(ii) In signing the application form where shown below, and in consideration of the receipt of this application by the Trust, the **Head of Department** UNDERTAKES that the information provided in the application form and otherwise in connection with this application is to the best of his/her knowledge and belief accurate and complete and that, in relation to any Award of Grant resulting from the application, he/she will:

6. Ensure compliance with the Trust's principles and policies on relationships between Trust-funded researchers and commercial entities as set out in Annex A to the Trust's grant conditions.
7. Consult with the Trust's subsidiary, Catalyst BioMedica Limited, prior to entering into an arrangement with any enterprise that will provide for the exploitation of any results arising from any activity funded under a Trust award.
8. Promptly inform the Trust of any material changes during the period of the Grant to any of the details provided in this application.

I have read the conditions under which grants are awarded and the undertakings detailed above and, if a grant is made, I agree to abide by them. I confirm that I have read and support this application, that I agree to this research being carried out in my department, and that all necessary licences and approvals have been or are being obtained.

Signature of Head of Department

Date:

(iii) In signing the application form where shown below, and in consideration of the receipt of this application by the Trust, the **Institution** UNDERTAKES that the information provided in the application form and otherwise in connection with this application is to the best of its knowledge and belief accurate and complete, and that it will:

9. Ensure compliance with the Trust's principles and policies on relationships between Trust-funded researchers and commercial entities as set out in Annex A to the Trust's grant conditions.
10. Consult with the Trust's subsidiary, Catalyst BioMedica Limited, prior to entering into an arrangement with any enterprise that will provide for the exploitation of any results arising from any activity funded under a Trust award.
11. Obtain from all individuals, subsequently funded as a result of the application, the equivalent undertakings as required from the **applicants *ab initio*** (i.e. before funding takes place).
12. Apply with full rigour all relevant arrangements for the protection of any patentable intellectual property rights arising from any research funded as a result of this application, as may from time to time be mutually agreed between Catalyst BioMedica Limited, the Trust's wholly owned subsidiary, and the Institution.. However, if the Institution decides not to proceed with the protection of any patentable intellectual property rights, it will co-operate fully (and ensure that its employees, students, contractors, and representatives co-operate) with Catalyst BioMedica Limited such that Catalyst BioMedica Limited will have an unreserved and unrestricted right, but not a duty, to seek patent protection.
13. Take full responsibility for the management, monitoring and control (including the requirements of all regulatory authorities governing the use of radioactive isotopes, animals, pathogenic organisms, genetically manipulated organisms (GMOs), toxic and hazardous substances, and research on human subjects and human embryos) of all the research work funded as the result of the application and all those staff (permanent, temporary and students) employed in or involved in any research funded as a result of the application.
14. Ensure that all permanent and temporary staff and students employed in or involved in the research receive training appropriate to their duties, in accordance with the regulations set down under the COSHH, ACDP and ACGM guidelines, the Health and Safety at Work regulations, and any other statutory or regulatory requirements as may apply from time to time.
15. Promptly inform the Trust of any material changes during the period of the Grant to any of the details provided in this application.

If a grant is made I will ensure that the funds provided are used for the purpose for which they have been given. I confirm that it is this Institution's intention to maintain its support for the department of the applicant[s] during the period for which this grant is requested.

I also confirm that this Institution *holds/is not required to hold a Certificate of Designation under the Animals (Scientific Procedures) Act 1986. I also confirm that I have read and I accept for and on behalf of the Institution the conditions under which grants are awarded and these undertakings.**

**Delete as appropriate*

Signature of Secretary of Institution/Finance Officer:

Date:

Position:

Institution:

Q6 SUMMARIES OF PROPOSED RESEARCH (no more than 400 words for both).

(a) For scientifically qualified assessors:

The proposed research program is a comprehensive, multidisciplinary investigation of the health consequences of rapid population aging in Latin America. The centerpiece of the program will be a longitudinal survey representative of the entire Costa Rican elderly population, complemented with a follow-up survey among Mexican elders. The Costa Rican survey incorporates cutting-edge measurement and research topics, including biomarkers of “allostatic load”, about which little is known in either Costa Rica or Latin America in general. Specific aims include: (1) To conclusively determine whether Costa Rican elderly longevity and active life expectancy is indeed superior to that of most developed countries. (2) To document differentials across time, regions, and countries in key indicators of health determinants and well-being, in order to generate hypotheses that will help set the future research agenda for these topics in Latin America. (3) To develop and test causal models of the inter-relations between behaviors and constraints across the life course, the availability of and burdens on social support and health systems, and ultimate effects on population health and longevity outcomes. Throughout this agenda the emphasis is on policy-relevant research designed to better target new interventions, as well as to influence debates throughout Latin America concerning appropriate responses to rapid population aging. The proposed program, which includes an important training component, will consolidate the development of a population research center of excellence in the University of Costa Rica, as focal point to disseminate population expertise to the Central American region.

(b) For readers who are not scientifically qualified:

Same abstract as above

NAME OF APPLICANT: Luis Rosero-Bixby

Q8 DETAILS OF RESEARCH PROGRAMME

i) **Aims of the program.**

The proposed program addresses the issue of the health and other consequences of population aging and its interrelations with social, economic, and institutional conditions. Population aging in upcoming decades is one of the major consequences of recent fertility declines in developing countries.

The program *main objective* is to determine the quantity and quality of life, and their determinants, among Costa Rican elders. It aims at validating earlier studies showing exceptionally high old-age longevity in Costa Rica, and to understand its determinants by tracing fundamental links with: (1) elderly intermediate health outcomes, 2) nutritional status, (3) behaviors through life course, (4) socioeconomic status, living conditions, and family support, and (5) health care access, utilization, and expenditures. Some collateral objectives are: (1) institution building of a regional population center of excellence for the study of demographic aging with a multidisciplinary scope; (2) diffusing to the region the skills, knowledge, and available information of this center by training specialists from other Central American countries and by consolidating its role as resource center; (3) to compare some of the results from this study with those from other countries to establish the uniqueness and commonalities of the Costa Rican case; a (4) to provide reliable information for policy decision making in the realms of retirement plans, demand for old age health care, support and living arrangements of the elderly, and the likes.

The *specific objectives* are:

1. To conduct a comprehensive survey in a nationally representative panel of about 8,000 Costa Ricans born before 1946, including in-depth health information in a sub sample of about 2,000 individuals, and follow-back interviews about the death. The panel will be followed until at least 2008 with provisions to continue following the panel afterwards.
2. To measure quantity of life expectancy (mortality patterns) and identifying some of their intermediate and final determinants.
3. To measure key biological indicators (biomarkers) of health status and health risks in the 2,000 sub sample, particularly those indicators that are part of the concept of "allostatic load" (Crimmins & Seeman 2001), as well as those of particular relevance for Costa Rica, such as *Helicobacter pylori*.
4. To determine the changes over time in survival status of the panel and in health functioning (biomarkers) of the sub-sample, as well as mayor changes in living arrangements and life styles.
5. To determine survival and its determinants in an existing sample of elders in Cuba and compare them with Costa Rica. Compare also the prevalence of key survival determinants with other Latin American countries that conducted surveys on aging.
6. To provide national and local officers with baseline estimates for implementing programs addressed to the elderly, including disability-free life tables, distributions of conditions such as high blood pressure, cholesterol levels, diabetes, obesity, and other risk factors.
7. To make the data of this survey readily available to the scientific community.
8. To provide master-degree training to at least four Central American students in a population and health program with a concentration in aging.
9. To provide short-term training on analysis of surveys on aging to about 15 Latin American professionals in an intensive workshop.

ii) **Background.**

Life expectancy in Costa Rica is almost 78 years, exactly the same as in the United States, the United Kingdom and Western Europe. It is the highest in Latin America, followed by Chile (77 years) and Cuba (76 years) and, by far, the highest in Central America, followed by Panama (74 years) (PRB 2002). Among adults, Costa Rican males in fact have higher age-60 life expectancy than even white males in the US (Brenes & Rosero-Bixby, 2002; Rosero-Bixby, 1995). This is despite Costa Rica having a per capita GNP of less than one-fifth that of the US (by purchasing power parity), and Costa Rica having per capita health expenditure of about one-tenth the United States (PAHO, 2002). Is this for real? If so, how can this be? In

fact, very little is known about longevity of the elderly in developing countries, much less longevity differentials and determinants. A 2000 United States National Academy of Sciences report (NAS, 2000), amply documents this lacuna, and forcefully argues the case for collection and analysis of longitudinal micro data on aging in developing countries.

Preliminary studies comparing causes of death have shown that the high life expectancy of Costa Rican adults come mainly from lower incidence of cardiovascular diseases, lung cancer and breast cancer. By contrast, Costa Ricans are in considerable disadvantage regarding diabetes mellitus, stomach cancer (one of the highest mortality in the world), and cervical cancer (Rosero-Bixby 2002). Little is known about socio-economic influences on adult health and survival. Some of these influences appear weak or even contradictory to the expected negative mortality gradient with higher socio-economic status (Rosero-Bixby 1995; Rosero-Bixby & Collado 2002).

As Latin American countries are completing their fertility transition, population aging is becoming a major concern (Martin and Kinsella, 1994). Costa Rica is at the leading edge of this process; since it had one of the earliest and fastest fertility declines in the region (Rosero-Bixby & Casterline, 1994). The country will reach fertility replacement levels by 2005. Population growth is consequently declining, except at old ages. The population aged 60+ will explode six-fold between 2000 and 2060--this is not mere speculation, given that this population was already born by the year 2000 (CCP & INEC, 2002). Similar situations will occur in most Latin American countries, with a lag of a few years. The challenges, and in some aspects opportunities, of this aging process are enormous. The demographic explosion of the elderly will affect policies related to health insurance, health care systems, health technology, pension benefits, savings, inter-generational transfers, and poverty relief. Health and social security systems in Costa Rica, and Latin America, are unprepared for this challenge.

Why Costa Rica? In addition to the fact that the country is leading the demographic and epidemiologic transitions in mainstream Latin America, there are three reasons that make Costa Rica an ideal setting for studying aging in the region. *First*, Costa Rica has among the highest quality vital statistics and other data registers of developing countries. This is extremely useful for tracking aggregate trends, but also as source of information to track individuals over time. Being a small country, it is feasible to conduct a national longitudinal survey with very low expected attrition. Yet the country, like the rest of Latin America, does not have any large population-based health surveys that can be used to understand the differentials and determinants of key aging constructs, much less have any panel data collection systems. *Second*, Costa Rica's health system is frequently cited as a model for other countries, but before lessons can be confidently drawn, micro data are needed to rigorously investigate the role of the health care system in contributing to the country's good health.

Third, Costa Rica is a unique outlier in terms of its high life expectancy. There is a rich scientific tradition of studying such outliers in order to draw paradigm-shifting inferences regarding causal determinants. Although some lessons from the study of outliers cannot be generalized due to their unique circumstances, there is little a priori reason to believe that Costa Rica possesses inherent characteristics that could not be replicated in other settings in order to improve longevity. The chance that lessons from Costa Rica may not be generalisable is vastly outweighed by the potential scientific benefits of learning from Costa Rica's good outcomes. Is the health status of Costa Ricans a direct result of access and use of particularly effective health care services? Is it a consequence of their life styles? Is it a result of past preventive interventions? The answers to such questions could have large implications for other countries as they allocate their resources across social sectors and across the life-course.

An important tool for studying such questions is the availability of high-quality, longitudinal household data gathered by multidisciplinary research teams. There are not, however, in our knowledge, significant examples of comprehensive panel studies on aging in developing countries (Taiwan is not a developing country) as the one in the proposed program that includes biomarkers, mortality follow-back interviews, and a two-country comparison. Important antecedents to our proposed research program are the multi-country studies on the well-being of the Elderly in Asia (Hermalin 2002); and the SABE study on Health, Aging and Well being in eight urban areas of Latin America and the Caribbean" (PAHO, 2001), which included a pilot survey in rural areas in Costa Rica (Dr Victor Gomez, the director of that study, is a co-applicant). These studies provide us a base of cumulative knowledge and experience in conducting cross-sectional surveys on aging. More substantively, these other recent surveys provide the opportunity for

cross-country comparative studies, which are invaluable both for generating hypotheses for further testing, and for understanding what lessons from Costa Rica may be generalisable. In order to further exploit this potential for cross-country comparison, we propose to conduct a longitudinal follow-up of the smaller-scale SABE survey in Cuba. By applying a comparable survey instrument to the longitudinal follow-ups, we will be able to greatly enhance the validity and potential for learning from such comparison.

iii) Scientific questions to be addressed.

Our research agenda focuses on multidisciplinary investigation of levels, trends, and relationships among four key sets of constructs as depicted in the conceptual framework in Figure 1: health behaviors and constraints over the life course, health stocks of the elderly, quantity and quality of life, and the health care system. General scientific aims can be grouped into three categories:

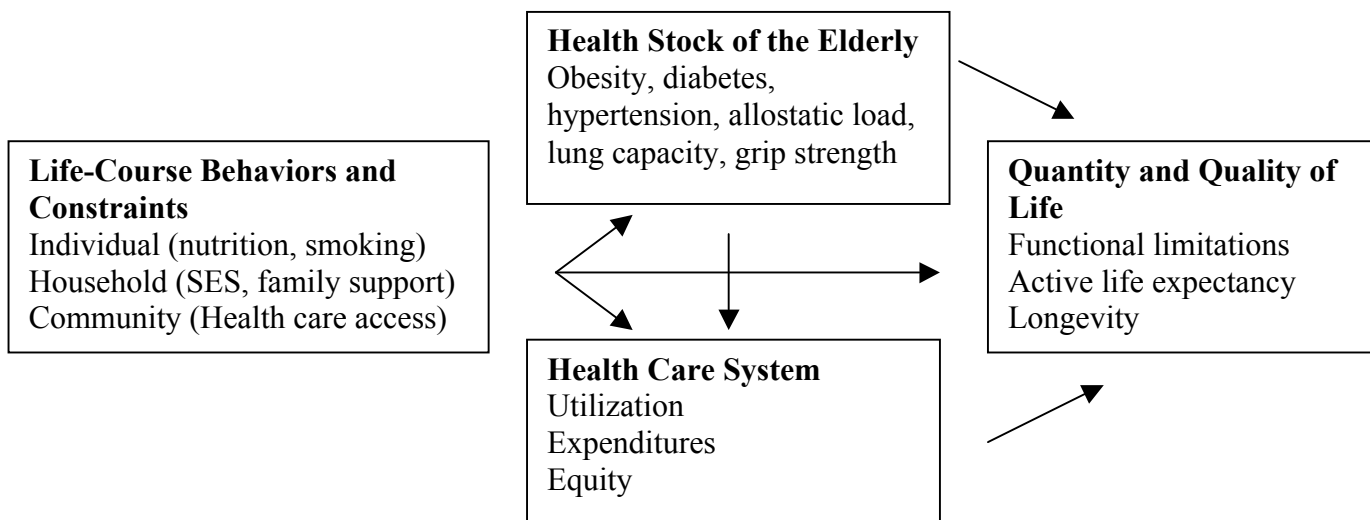


Figure 1: Conceptual framework depicting causal directions of interest among major constructs.

- *Establish key stylized facts.* Even the most basic facts concerning levels and trends among the elderly for many of our constructs are not well known in Costa Rica or in Latin America more generally. Creating such knowledge is important for many ends, including for the purposes of effectively prioritizing and targeting programmatic interventions.
- *Hypothesis generation.* Descriptive analysis of multivariate associations (both within and between countries) among our main constructs is a crucial step in generating hypotheses to address the fundamental scientific question: Why does Costa Rica have such good health outcomes relative to its aggregate inputs, and what lessons can be learned for other countries?
- *Causal modeling.* The final step in this research agenda is to identify which of the observed relationships truly reflect causal pathways that could be manipulated by public policy. The creation of longitudinal data with a rich array of individual, household, and community level variables is critical to developing the causal models, which must underpin evidence-based policy for the elderly.

Our first set of scientific questions relates to establishing the key stylized facts regarding Costa Rican longevity: Is the high life expectancy of Costa Rican adults real or just an artifact of poor-quality data (under-registry of deaths and/or population over-count due to age misreporting in the census)? How does the old (and very old) age-pattern of mortality in Costa Rica compare to other countries, especially Cuba? The study of mortality at very old ages (90 and higher) is the object of intense scrutiny in current demography (Horiuchi & Wilmoth 1998; Oeppen & Vaupel 2002); thus far the debates have been based exclusively on data from developed countries. By generating high quality data on observed mortality experiences for individually-tracked cohorts, our research program will enable the scientific community to better analyze the causal determinants of longevity in Latin America as well.

A second set of questions has to do with the health-related quality of life (Feasley 1996) of elderly Costa Ricans. Does their functional health status compare to other countries as advantageously as their life

expectancy? To what extent are quantity and quality of life interconnected, as reflected by healthy life expectancy? In order to distinguish long-term frailty from short-term health shocks, it is essential to have longitudinal data in which the speed and trajectories of disability decline can be measured from multiple observations of individuals at different time points prior to death.

A third set of scientific questions seeks to identify life course behaviors and constraints, which serve as potential proximate and distal determinants of health outcomes. This requires measurement of a wide array of individual, household and community-level variables conceptualized in a multidisciplinary framework. The community-level variables will include indicators of both financial and geographic access to health care, rigorously measured by using GIS tools to link households to health facilities. Household level variable will include socioeconomic status and family support, which are also interesting in and of themselves as indicators of the social well-being of the elderly.

A fourth set of questions relates intermediate and eventual health outcomes to these individual, household and community variables. This will include the study of important health determinants such as nutrition, and smoking, as well as other behaviors such as labor force retirement, in addition to effects of community health care access. Intermediate health outcomes include traditionally important mortality risk factors such as obesity, hypertension, and diabetes, as well as a richer array of biomarkers including peak-flow lung capacity, and grip strength. Most innovatively, we propose an extensive analysis of the role of stress as it relates to these other variables. To operationalize the stress construct, we will use the concept of “allostatic load” as an integrative model of physical functioning and biological risk (Seeman et al, 2001). This concept of allostatic load has been developed in the last decade by the MacArthur Studies of Successful Aging (Seeman et al 2001), and has proved to be an innovative new approach for characterizing the wear and tear that the body experiences due to life circumstances and body responses to maintain stability (allostasis). It has been defined as “the cumulative physiological toll of dysregulation across multiple systems over time, reflecting both a multi-system and life-span orientation, and is hypothesized to affect subsequent mortality, disease pathology, and aging.” (Crimmins & Seeman 2002:25). In particular, we will test the hypothesis that a summary index of allostatic load is an important predictor of survival and other health outcomes in a Latin American population.

Fifth, we propose to study how the changing health of the aging population affects the provision of social and health services in transitional societies such as Costa Rica. What are the patterns (including spatial patterns) of health care utilization among Costa Rican elders? Perhaps more importantly from the perspective of strategic planning within the health sector, how does utilization change with age, as opposed to the time until death?

To reiterate, some scientific elements that set apart the proposed study from others made in Latin America and developing countries are: the coverage of rural populations (SABE was mostly urban), a longitudinal or panel design, collection of biomarkers and its summary-- the allostatic load index, a follow-back interview about the death, the follow up of survival in a larger sample, during longer period and with enough statistical power to determine mortality rates at very old ages.

We believe that this survey, unique in Latin America, will become a major resource for multi-disciplinary analyses of the consequences of population aging, much like the Health and Retirement Surveys in the US, UK, and other developed countries. The multi-purpose questionnaire, extensive health measurements, administrative data linkages, and particularly the panel design will enable a rich array of scientific studies with direct policy relevance.

iv) Description of study design and methodology.

A US-NAS report (2000) makes 6 overarching recommendations necessary for research to address policy issues related to population ageing: (1) Develop multidisciplinary research designs, (2) Collect longitudinal data, (3) Harmonize data collections across countries, (4) Conduct comparative cross-national research, (5) Develop linkages across in-country databases, and (6) Make data publicly available for research. Our research will advance the Latin American scientific frontier in all of these dimensions. Specifically, we propose a longitudinal research design with the following components:

Component 1. Tracking a national sample of 8,000 Costa Ricans born in 1945 or before, using previously validated comprehensive computerized databases of vital registration, voting, and public pension records. This sample already exists from a study of life tables for the elderly that we conducted by request of

the national authority on pension and retirement programs (Brenes & Rosero-Bixby, 2002). We drew the sample from the 2000 census database and the census office (INEC) provided us the names of these individuals, which, in turn, allow us to link them to the voting, vital registration, and pension databases. We over sampled older individuals in order to have an appropriate representation of the very old (age 90 and above). We have the identification and address for these individuals, as well as their 2000 census record and birth certificate. We have already followed them for 2.5 years identifying more than 800 deaths and conducting preliminary analyses of socioeconomic determinants of survival at old ages (Rosero-Bixby & Collado 2002).

Component 2. Conducting a multidisciplinary survey in a clustered sub-sample of about 3,000 survivors drawn from the aforementioned sample. Interviews, which will take place 5 years after the census on the average (2004 to 2006), will be conducted in-person at their homes, allowing measurement of a battery of objective, clinical health indicators to supplement self-reported health status and activities of daily living (Murray et al., 1995). These will include measures such as anthropometry, hypertension, cholesterol, diabetes management, and a mini-mental test. In addition to health indicators, we will collect information on socioeconomic characteristics, living arrangements, and use of health care. Socio-demographic changes since the census will also be measured. The questionnaire to collect self reported information would be adapted from the SABE study (this will allow comparisons with seven other countries). This is a comprehensive, two-hour questionnaire that includes the following topics or modules:

- Socio demographic characteristics, including living arrangements;
- Self-assessment of chronic and acute illnesses;
- Self-assessment of physical and mental impairments and disability;
- History of principal chronic conditions;
- Access to and use of health care;
- Family and kin support;
- Anthropometric measures (height, weight, grip strength, skinfolds waist and calf circumference);
- Physical limitations (standing on one foot, bending and crouching, walking), and
- A mini-mental test.

In addition to the anthropometric and self-reported measures, the household survey will collect blood (two 5 cc tubes, one with serum separator and the other treated with an anticoagulant), overnight urine and measurements of blood pressure and pulmonary function (peak flow rate). This collection effort will allow us to measure the following biomarkers (most are part of the allostatic load index):

- Body-mass index and waist-hip ratio (an index of metabolism and adipose tissue deposition; Bjorntorp, 1987, Krauss, et al 2000);
- Systolic and diastolic blood pressure (indices of cardiovascular activity, Seeman, T, Berkman, L, Blazer, D & Rowe, J (1994))
- Peak flow rate (a measure of lung function) (Cook, N, Evans, DA, Scherr, FE, Speizer, JO, Taylor; JO & Hennekens, CH 1991)
- Glycosylated hemoglobin (HbA1C; an integrated measure of glucose metabolism over previous 30-90 days; Koenig et al, 1976; Dunn et al, 1979, Peters AL, Davidson MB, Schriger DL, Hasseblad V (1996) . HDL/LDL and total cholesterol (markers known to influence cardiovascular diseases, including the development of atherosclerosis, NCEP,2001)
- Serum dihydroepiandrosterone sulfate (DHEA-S; a functional HPA axis antagonist; Svec & Lopez, 1989)
- Urinary cortisol excretion (a measure of 12-hr Hypothalamic Pituitary Adrenal HPA axis activity)
- Norepinephrine and epinephrine excretion levels (a measure of 12-hour Sympathetic Nervous System activity Seeman & McEwen,1996)
- Insulin secretion as indicator related to glycosilated hemoglobin and metabolic control.
- Creatinine clearance as renal functioning indicator and closely related to hypertension control.
- C Reactive Protein as an inflammation indicator which has been closely associated with functional disability and mortality (Reuben,1999)
- Antibodies to Helicobacter Pylori (probable agent for stomach cancer, Sierra,1992)
- Fatty acids content in erythrocytes as an indicator of dietary intake. (Kagambe et al. 2000)
- Antioxidants (folic acid B12 vitamin, which are related to cardiovascular diseases, some types of

cancer, longevity, and cognitive functioning)

- Standard CBC, including hematocrit and hemoglobin
- Fasting glucose

Additionally we will be conducting dietary interviews to a nested population using a semi-quantitative food frequency questionnaire (FFQ- Kagambe, et al 2000) to identify nutrient intake trends related to metabolic syndrome and mortality.

Two field teams, each integrated by a driver, a laboratory technician/phlebotomist, and 2 interviewers will collect the information and specimens in the households. We expect the team will complete 16 interviewees per week on the average, in order to complete the first round of visits to 3,000 individuals in two years. The second round will require a lower effort, which allow for tracking individuals who moved and the death's descendants.

We plan to conduct computer-aided interviews (CAI) using handheld computers (palmtops), instead of the traditional paper and pencils. The CCP is currently developing and testing this new technology, which will allow improving data quality and feedback timing.

Other technological innovations we plan to use are barcodes to identify individuals and specimens (palmtops can read them), and GPS devices to take the exact geographic coordinates of households and health facilities.

The laboratory tests will be conducted through the Research Program on Ageing at the Institute for Health Research (INISA) of the University of Costa Rica, which is a collaborating center in this study.

Component 3. Conducting an abbreviated resurvey two years later (seven years after the census) to capture the changing dynamics of health and living conditions among survivors of the 3,000 sub sample (expected N = 2,300). We will develop a shorter questionnaire for this follow up visit, similar to the one we will use in Cuba (component 5). We will take again the Biomarkers to compare them with those taken two years earlier.

Component 4. Conducting a follow-back interview among relatives of those in the sub sample who died in the follow up period to determine the events that preceded death, especially health care utilization (a group in the Ministry of Health has ample and successful experience auditing all infant deaths in the country). Health service use at the end of life accounts for a large proportion of health expenditures in many high-income countries (Zweifel et al., 1999), and our follow-back survey will provide a unique resource for exploring this critical issue in a less developed country with lower health expenditures.

Component 5. A follow-up re-survey of the 1,500 Cuban elders included in the SABE study to determine survival status and major changes in health and living conditions 5 to 6 years after the first interview. We implement this component in collaboration with the *Centro de Estudio de Población y Desarrollo* (CEPDE) of the *Oficina Nacional de Estadísticas* and PAHO, which were the organizations in charge of the SABE study in 1999-2000.

Sample design

The study panel will be a sample of about 8,000 Costa Ricans aged 55 and above in June 28, 2000—the census date. We already drew this sample directly from the census database with a probabilistic, age-stratified design, aiming at having 1,200 individuals in each of the five-year groups from 55 to 84, and 400 individuals in the groups 85-89, 90-94 and 95-98. We took the entire population (359 people) in ages 99 and above. Foreigners (about 5%) were taken out of this sample, since they cannot be followed through the vital registration system (they do not have an identification number). Table 1 shows the sample size by age group and the corresponding expansion factors. Note there is over-sampling at older ages to provide statistical power to study the very old. Table 1 also shows the death rates of this sample in the first 2.5 years of follow up.

The 3,000 sub-sample for the household survey will be taken from the about 6,000 survivors of the aforementioned survey. In order to have a clustered sub-sample that will facilitate field work, we select health areas (or cantones where health areas do not exist) with probability proportional to size. We aim at interviewing to at least 90% of surviving individuals of the original sample with residence in the selected areas at the time of the 2000 census.

We will also take an inventory of the health facilities existing (about 300) in the areas included in the subsample.

Table 1. Sample size by age in the longitudinal study of Costa Ricans elders

Age at 2000 census	Census population	Sample	Expansion factor	Death rate*
Total	387,572	8,368		53.1
55-59	99,533	1,122	88.7	10.3
60-64	83,912	1,138	73.7	10.5
65-69	68,487	1,165	58.8	16.6
70-74	55,256	1,114	49.6	24.9
75-79	36,698	1,124	32.6	41.5
80-84	22,578	1,126	20.1	65.0
85-89	14,101	385	36.6	104.9
90-94	5,302	402	13.2	171.0
95-98	1,346	433	3.1	241.1
99 & +	359	359	1.0	366.1

* Annual rate for the period 2000-2002, per 1,000 people.

Envisioned problems and concerns

The major challenge in a longitudinal study is attrition, which can compromise representativeness. Although attrition will not affect the follow up of the full panel through computer records it can be a problem in the 3,000 sub-sample. The effect of attrition is, however, expected to be lower than in studies on young adults, since mobility among the elderly is lower. According to the 2000 census, 7% of individuals 60 and over changed their municipality of residence in the previous 5 years. The small size of Costa Rica (50,000 km². 4 million inhabitants) allows to track those who move, which we intend to do for expected 150 individuals in the first survey visit and 50 in the second visit. By the same token we expect to track the descendants of the about 200 deaths between the two visits for the follow-back interview.

High no-response and rejection rates can also compromise representativeness. Although in Costa Rica this has not been an important problem so far, especially at old ages, we will aim at improving cooperation by providing immediately some results of blood tests and food intake assessment as token gift to participants. We expect to keep non response below 10% for the questionnaire interview and 20% for blood and urine specimens.

The principal investigator has the experience of directing a case-control study on cancer and contraception, which implied specimen collection and tracking individuals throughout the country (Rosero-Bixby et al 1987; Lee et al 1987; Oberle et al 1988; Erwing et al 1988)

The small sample size, especially for the 3,000 sub-sample, will certainly limit the statistical power in some analyses of low-prevalence or incidence conditions. We will report as far as possible sample errors and will be careful in picking only study topics for which we will have enough statistical power. The high cost and complexity of panel studies do not allow to have large sample sizes.

The generalisability of Costa Rican results may be questionable. This is true for any one-country study. The only way of avoiding this problem would be with a multi-country study which is not feasible. Instead, we will make every efforts to have comparative cross-section results with those from the SABE survey in Latin American and the Michigan-lead survey in Asia. We are also including in this proposal a survey in Cuba and use the longitudinal results of the MHAS Mexican Survey currently under way. These surveys will allow us to compare survival patterns and their determinants, as well as other longitudinal changes in Costa Rica, Cuba, and Mexico and to have a sense of the "uniqueness" of Costa Rica.

v) Dissemination / Outcome of Research Findings:

a) What are the likely outcomes / impact of the proposed research?

This panel survey is designed to allow multidisciplinary study of a wide range of research questions of central importance to Latin American's rapidly aging population. The first hypothesized research finding is that we will be able to firmly establish that Costa Rican elderly longevity is indeed superior to that of most

developed countries. This itself is likely to have an important impact on the global health community's understanding of the most important determinants of adult health. Second, we plan to document the levels of numerous mortality risk factors and health determinants in this population. We expect this to generate controversial hypotheses regarding the relative importance of various health determinants, and hence help set the agenda for future research on elderly population health in Latin America. Third, our rich multidimensional measures of elderly health and well-being, and the trajectory of changing well-being near the end of life, will provide essential data necessary for designing well-targeted interventions. We plan to work closely with government health and aging organizations in disseminating these results, to enable this research to also have substantive near-term impacts benefiting this population. Fourth, our research is designed to assess the current and potential future burdens of population aging on both formal and informal social support systems, ranging from the health services sector to family caregivers. Our data will provide unique information critical for planning rational policy responses to an aging population, and we plan to disseminate findings from this policy-relevant research agenda to a wide range of stakeholders influencing debates over health and social policy. Finally, high quality innovative surveys inevitably lead to unexpected contributions in new research areas. By incorporating a rich array of cutting-edge measurement and research topics in this data collection system, and making public use data files easily available to the wider international research community, we have high additional expectations for the longer term unpredictable benefits that will arise from this research program.

b) How would the findings be disseminated?

One of the strengths of CCP is dissemination of population information and data. The Center's Internet servers are the main vehicle for this. Our conferences and workshops are also settings for disseminating research results. We intend to use all these vehicles, in addition to scientific publications and conference papers. Some of the specific activities we foresee are: (1) web pages with the program results, data and methods. (2) Taking part in the network of SABE centers to exchange experiences. (3) Organizing at least a session in a major professional meeting in Latin America and either in a IUSSP conference or a PAA meeting (the principal investigator has organized this kind of sessions several times in the past). (4) Making the databases available to the scientific community throughout the Center's Internet data servers for online processing (5) Conducting, in 2008, an international workshop on analysis of surveys on aging, which will be a longer and improved version of the workshop we already offered in 2002 in collaboration with PAHO and the Fogarty Center in the University of Wisconsin.

c) How might the findings be incorporated into public health policy / practice.

Mostly with the program links with the National Council on Senior Citizens, supervising authority of the national pension system (SUPEN), as described in the following section. This is the highest authority on policies for the elderly population in Costa Rica. We have already contacted the Council, which is enthusiastic about the possibility of the proposed research program. Enclosed letter of support of this Council.

vi) Local and Regional Links:

- This proposal has the support of the National Council on Senior Citizens, which is the highest office in charge of policies for the elderly in Costa Rica (enclosed letter of support). We intend to work in close contact with this Council, providing it information for decision making on demand, as well as keeping it informed of policy-relevant findings of this program.
- With the "Colegio de la Frontera Norte" in Tijuana, Mexico. The Center's director, Dr. Ham-Chade, is co-applicant in this proposal. He was the director of the Mexican SABE study and he will be in charge of the follow up survey of Mexican elders we are proposing.
- With the research programs on Ageing and on Gastric Cancer of the Institute for Health Research (INISA). The Cancer Program director, R. Sierra, is a collaborator in this proposal.
- With at least three ongoing research projects in CCP: (1) determinants of heart disease in Costa Rica, (2) demography of poverty, and (3) use of palmtops for data gathering in the field. The directors of this projects (Campos, Barquero a, and Antich are collaborators in this proposal)

- With the three other members of the Fogarty Center, which we participate in: CEDEPLAR in Brazil, El Colegio de Mexico, and the University of Wisconsin. We will receive visiting scholars from these centers to learn and exchange experiences on research on aging.
- With PAHO and the seven Centers that conducted the SABE survey in Latin America.
-

vii) **Joint applications and collaborations**

Xinia Fernández, Ph.D., co-applicant, from the Institute of Health Research (INISA) of the University of Costa Rica, will bring to the program her expertise in nutrition epidemiology and biomarkers and dietary data collection and analysis. She will be based in INISA taking care biomedical analyses. As the director of the Research Program on Ageing in INISA, she will bring the expertise developed in that program in several studies of healthy aging conducted since 1987. Dr Fernandez just returned to Costa Rica after completing her PhD in Indiana University. The possibility of participating in a major research program as this one, will be crucial for her re-insertion into the University and to avoid the brain drain that often occurs out of frustration among those trained at doctoral level abroad.

William Dow, Ph.D., co-applicant, from the University of North Carolina, will bring to the program his knowledge on health economics and the experience and resources from his NIH R01 grant on "Economic Determinants of Mortality" (a comparative analysis of the US and Costa Rica) in which we have been collaborating for four years. He intends to bring new NIH grants to the program in the future to study the economic determinants of health.

The following collaborators are CCP research staff members: J.C. Vargas, M.Sc., Anthropologist, will bring his expertise in field work and data collection; J. Barquero, M.Sc., sociologist and demographer, will analyze data on poverty and bring his expertise from his ongoing project on demography of poverty; C. Marin, MPH, MD, will be in charge of safety monitoring and feeding back results of laboratory tests to participants; Daniel Antich, M.Sc., computer science expert, will be in charge of data processing and will bring the expertise from his ongoing project in the use of palmtops for data collection; and G Brenes, M.Sc and Ph.D. candidate, statistician and demographer, will bring his expertise in statistics and mathematical modeling; he intends to base his PhD dissertation in this program.

Hannia Campos, Ph.D., collaborator, research associate of CCP and Professor at Harvard University, will bring her knowledge on nutrition and her experience and resources from her several NIH-R01 grants to study gene-diet interactions and heart disease in Costa Rica. She will also advise us about data collection and analyses on diet and to identify whether specific individual fatty acids protect against incidence of metabolic syndrome.

Rafaela Sierra, M.Sc., collaborator will bring the resources and expertise from her research program on gastric cancer epidemiology in INISA. Her team has developed a serologic method for detection of *Helicobacter Pylori* infection. She will contribute with this laboratory test and the analysis of prevalence of this infection.

Fernando Morales MD is the director of the Blanco Cervantes hospital for the elderly and president of the National Council on the Senior Citizens, which is the highest office in charge of policies on the elderly. He will advise the program in policy issues and will be the link with the National Council for translating research findings into policies.

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Q10 RESEARCH TRAINING AND STRENGTHENING OF RESEARCH CAPACITY

Please provide a detailed description on how you intend to incorporate this aspect into the proposed programme or research (maximum 1 page).

The Central American Population Center (CCP) hosts an international master's degree in population and health, which has trained 40 population specialists (plus a current cohort of 14) mostly from countries other than Costa Rica. It has also upgraded the skills of 138 population professionals from 18 Latin American countries in 10 international workshops in the past 4 years. In addition, more than 100 population scholars have met in three international conferences/seminars hosted by the Center in 1995, 1996, 1997, 1999, and 2002 (two more are scheduled in 2003). The research projects in CCP have enriched importantly these training activities, especially the master-degree program. Many master's trainees are involved in internships or assistantships in Center's research projects or use the Center's databases in their theses and term papers. CCP's research projects are thus training laboratories that complement the work in the classroom.

Having a major research program such as the one we are proposing here will greatly strengthen the hands-on training base of the Center and, consequently, its training capacity. Moreover, we are specifically requesting funding to bring eight fellows from other Latin American countries for training in the Center's Population and Health Master-degree program, which has a duration of less than 2 years. Using the infrastructure of the proposed program we will open a concentration in aging as part of this master-degree. These eight Master fellows will participate in the proposed research program as part of their required internship and graduation thesis.

The proposed program also includes the organization of two two-week international workshops to train 20 to 30 Latin American researchers on the analysis of survey data about aging in 2006 and 2008 (the CCP in collaboration with PAHO and the University of Wisconsin already conducted one such workshop in August 2002). We are requesting fellowships to bring in each workshop 7 participants from abroad (others will come with their own funding), as well as two instructors.

As a third training component we are requesting funding for a six-month training internships in "El Colegio de la Frontera Norte", Tijuana, Mexico. A CCP researcher would spend 6 months in El Colegio in 2004, learning from the experience in that Center with the SABE study, as well as analyzing the MHAS data, under the supervision of Prof. Ham-Chade, collaborator in this proposal. This fellow will also conduct analyses of the pilot-SABE in Costa Rica, to draw conclusions for the panel study.

A fourth training component is the PhD dissertation project of Gilbert Brenes, a bright research staff member of CCP, under training in the University of Wisconsin, Madison, since 2002. Mr. Brenes is a collaborator in the proposed program. The program will fund a three-month stay of Mr Brenes in Costa Rica to participate in the research effort and take the data needed for his dissertation. In this way, we hope to keep Mr. Brenes linked to Costa Rica and the Center to insure his return after he completes his PhD.

Q11 PARTICIPATING INSTITUTION(S)/ORGANISATION(S)

The Central American Population Center (CCP) of the University of Costa Rica (UCR) will implement the proposal. The Foundation for Research of the University of Costa Rica (FUNDEVI) will administer the funds. Two major collaborating centers will be the Institute for Health Research (INISA) of the UCR in charge of handling the biological specimens and coordinating laboratory tests, and “El Colegio de la Frontera Norte” of Tijuana, Mexico, in charge of the Mexican follow up survey (UCR will subcontract to El Colegio). The following description refers only to CCP

i) **Source of funding for the institution.**

Core CCP funding comes from UCR budget (professor’s salaries and services like electricity). Staff researchers and support personnel are hired for specific projects or funded by center grants. The Center’s budget for 2003 is about US\$ 700,000: 16% from UCR budget, 9% from income generating activities, and 75% from external grants. The major external donors are the Mellon, Gates and Hewlett Foundations, as well as the USAID-funded, MEASURE project in the University of North Carolina.

ii) **Existing partnerships & links in the region.**

Apart from the collaboration with several US centers and the support from US-based foundations, CCP is member of a Fogarty Network of three Latin American centers (Colegio de Mexico, CEDEPLAR in Brazil, and CCP). The network conducts joint activities mostly in population training. As part of it, CCP hosted a Latin American workshop on analysis of surveys on aging and it sent to Wisconsin for PhD training to one of its junior researchers and it will send another this coming year. CCP is also active member (and the node for Central America) of the IPALCA network of population libraries in Latin America.

CCP has active cooperation agreements with the “Universidad Centroamericana” in Nicaragua for research on transmigration between the two countries, as well as with the “Colegio de la Frontera Sur” in Chiapas for research in reproductive health and training in impact evaluation. For implementing the current proposal, CCP will work in close relation with “El Colegio de la Frontera Norte” in Tijuana.

CCP also has signed agreements with the National Statistical offices in Costa Rica, Panama, Nicaragua, and Belize and with the National Cancer Registry in Costa Rica to provide free, online access to their census and other population databases.

CCP is in charge of providing to the newly created National Supervising System of Pension Funds (SUPEN) with the official life tables of Costa Rica for actuarial purposes.

iii) **Briefly describe any current research programme(s) with potential for synergy.**

The UCR established the CCP in 1993 to fill the breach left by the closing of CELADE-San Jose, a UN regional Center in demography. The Program became a “Center” in 2001. In that year it also built its own premises with support by the Bill and Melinda Gates Foundation. The Center has become a leading organization for population research and training in Latin America in a time when other population Centers in the region were scaling down activities or even disappearing. Its population library is unique in Central America. A core of highly qualified demographers, with advanced degrees from world-class universities, is the Center’s most important asset. Its Internet servers and web pages are required destinations for those seeking information on population in Central America (<<http://ccp.ucr.ac.cr>>, <<http://censos.ccp.ucr.ac.cr>>, and <<http://encuestas.ccp.ucr.ac.cr>>). No other Center in the world offers online processing of full population censuses as the CCP does (it currently has 8 censuses online and the number is growing). The center has (or had) research projects in such topics as population and deforestation, transnational migration, access to health services, aging, adolescent fertility, factors of heart disease. As recognition of its accomplishments, the Center has signed agreements or received grants from local agencies and, especially from international organizations such as UNFPA, PAHO, WHO, USAID-funded Measure projects, as well as from the Mellon, Hewlett, Rockefeller, Gates and Compton Foundations. In this way it has created a de facto alliance of donors seeking to improve population research and training in Central America.

As indicated in section vii) of the research protocol, the proposed program will collaborate with several ongoing research initiatives in CCP (demography of poverty, diet and hearth disease, use of palmtops), in INISA (programs on aging and cancer), as well as projects on health economics of Dr Dow in UNC and Dr Ham-Chade on aging in El Colegio de la Frontera. These projects and programs will mutually benefit from the collaboration.

Q12 MILESTONES OR DELIVERABLES are crucial in providing periodic checks on progress to ensure that your project is on track and thus successful continuation of the proposed work. Please set appropriate quantifiable milestones / goals to serve as bench marks for success / progress of your project, and state how these might be measured:

Q12 MILESTONES OR DELIVERABLES

Year 1

- Premises and equipment are procured
- Personnel is hired and trained
- Fieldwork planning is completed (including a full pilot study, questionnaires in palmtops, field procedures, subsample selection)
- Collaboration agreements are established for laboratory tests
- Linkages are formally established with National Council for the Elder Population
- Collaboration from local public health facilities is procured at the Central level (Ministry of Health and Social security)
- Four Master-degree fellows are recruited
- 25% of the first-round fieldwork is completed

Year 2

- Subcontract for conducting the Cuban survey is signed
- Fieldwork planning of the Cuban survey is completed
- 25% of the fieldwork in Cuba is completed
- 75% of the first-round fieldwork in Costa Rica is completed
- First computer follow up of the full sample is completed after 5 years from the 2000 census
- Proposal for PhD dissertation in Wisconsin is approved

Year 3

- First round of the Costa Rican subsample survey is completed
- Cuban survey is completed
- Preliminary analysis are conducted and results presented in a scientific meeting and at the National Council for the Elder
- The first workshop to compare cross-section data is implemented.
- A Web page with program's results and data is implemented
- Four master fellows complete their training and 2 new master fellows are recruited
- Preparation for the second round are completed, including the follow-back of the death
- 25% of the second round fieldwork is completed

Year 4

- 75% of the second-round fieldwork is completed
- Mr. Brenes return to Costa Rica after completing his PhD
- First publications with results from the computer follow up, the first-round subsample, and Cuban survey
- We organize a session on ageing in Latin America in a major scientific meeting (e.g. PAA)

Year 5

- All fieldwork and lab tests are completed
- The 2-week international workshop takes place.
- Two Master fellows complete their training
- A comprehensive program's report is presented to local authorities
- At least two scientific articles are submitted to international journals.
- A proposal to continue following the panel is approved and funded.

Q13 RESEARCH ON HUMAN PARTICIPANTS OR HUMAN TISSUE

- (a) Does your project involve the use of human participants or human tissue? YES NO

If yes, refer to notes. Please state in appropriate detail (and provide written evidence where relevant) any permission which you have and the title of the Ethics Committee which gave it.

- (b) Does your project involve the use of human embryos requiring a licence from the Human Fertilization and Embryology Authority (HFEA)? YES NO

If yes, refer to notes. Give licence number, date of issue, end date and title of approved project.

- (c) Does your proposal involve research on gene therapy which requires regulatory approval? YES NO

If yes, refer to notes.

Q14 EXPERIMENTS ON ANIMALS

- Do your proposals involve the use of animals or animal tissue outside the UK? YES NO

If yes, give details of the local ethics committee approval that has been sought, relating this approval to the permission which would be required if the research were to be conducted in the UK.

Q15 COMMERCIAL EXPLOITATION

- (a) Will the proposed research use technology, materials or other invention that, as far as you are aware, are subject to any patents or other form of intellectual property protection? YES NO

If yes, give brief details.

- (b) Is the proposed research, in whole or in part, subject to any agreements with commercial, academic or other organizations? YES NO

If YES, give brief details.

- (c) Is the proposed research likely to lead to any patentable or commercially exploitable results? YES NO

If YES, give brief details.

- (d) If any potentially commercially exploitable results may be based upon tissues or samples derived from human participants, please confirm that there has been appropriate informed consent for such use.

NAME OF APPLICANT:

Q16 CONSULTANCIES AND EQUITIES

Do any of the applicants have consultancies or any equity holdings in companies or other organizations that might have an interest in the results of the proposed research? YES NO

If yes, refer to notes and give brief details.

Q17 RELATED APPLICATIONS

(a) Is this or a related application currently being submitted elsewhere? YES NO

If yes, to which organization?

By what date is a decision expected? (dd/mm/yyyy)

(b) Has this, or a similar, application been submitted elsewhere over the past year? YES NO

If yes, to which organization?

What was the result?

(c) What proportion of working time do the Principal Applicant and Co-applicant(s) spend on research? (%)

What proportion of this time will be spent on the project by the Principal Applicant and Coapplicant(s)? (%)