Malaria survivors during early life, health at old age, and stroke mortality in Costa Rica.

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Abstract

Mortality decline was more recent and more rapid in developing countries than in industrialized countries. Current elderly people in developing countries were exposed to a deleterious health environment during their early years. In Costa Rica, 11% of people aged 60 and over in 2004 reported that they had malaria during their youth. These malaria survivors constitute a selected population given that they survive the disease; however, there is evidence that these survivors might be more likely to have cerebro-vascular diseases (stroke) at adult ages. The aim of this article is to use the CRELES study (a study about aging in Costa Rica) to determine how different are malaria survivors compared to the rest of the Costa Rican elderly, and determine whether they are more likely to die due to stroke, to cardiac diseases (which are related to exposure to infections at early ages), or to other causes of death. We find that malaria survivors are on average of lower socioeconomic status. However, the prevalence of several morbidities is not significantly different between malaria survivors and the rest of the elderly population. Malaria survivors are more likely to die due to stroke, but not due to other selected causes of death.

Introduction.

The world has observed a fast mortality decline during the last 150 years. This decline has occurred in a fraction of that time in developing countries like Costa Rica. This country has gained notoriety for achieving very high life expectancy at birth similar to that observed in European nations. Rosero-Bixby (2008) even claims that Costa Rican elderly males are the longest living human beings. This author acknowledges that this finding might be explained by the fact that elderly Costa Ricans are a selected population composed of cohorts that survived an environment characterized by a high incidence of infectious diseases, maternal mortality and malnutrition, limited availability of health and education services, and widespread poverty. These characteristics are at the core of evolutionary bio-demographic arguments: The components of population change are related to population composition, which in turn can be determined by differential survival.

Malaria is one of the most prevalent infectious diseases in the tropics. In Costa Rica at the beginning of the 20th century, malaria was one of the most important causes of mortality and morbidity even among children. Even though malaria is highly lethal –its accepted lethality rate

is around 20% ()–, an important proportion of the Costa Rican population born during that time did survive the disease. This survival might be explained either by the "variety" of the disease or by the age at infection (buscar).

Malaria –as well as other infectious diseases, like Chagas disease, cysticercosis, and gnatostomiasis– are known risk factors of stroke morbidity and mortality in the tropics (Carod-Artal, 2007; Gomes and Chalela, 2005; Leopoldino, Fukujima and Gabbai, 1999). Although most of the scientific evidence links malaria with stroke mortality short after infection, it is possible that malaria survivors might be at higher risk of cerebro-vascular accidents through their life course, due to the degenerative effects that this infectious disease might have on brain tissue (Desruisseaux et al., 2010). Such long-term effects are typical of other diseases, like Chagas disease and congestive heart disease.

The aim of this paper is to assess whether elderly Costa Ricans that survived malaria during their early life are at a higher risk of dying due to cerebrovascular causes at old ages, when compared to those who did not suffer the disease. Another goal is to study differentials in health indicators between these two groups in order to understand how different (or selected) the malaria survivors are with respect to the rest of the population.

Biodemography and mortality at old ages

The reductions of late-age mortality have augmented the interest on the biodemography of aging during the last two decades. After medical, technological and public health advances, as well as improving socio-economic standards of living made it possible to reduce the incidence of premature deaths (those caused by several preventable diseases and injuries) in low mortality populations, senescent deaths, research on aging has increasingly focused on senescence: "a progressive increase in age-specific death rates even under ideal conditions" (Carey and Judge, 2001, p.12). Several notorious findings of biodemographic research have convinced researchers that senescence could be postponed. Among these findings, Vaupel (2004) mentions that a mortality plateau has been observed at very old ages in high life expectancy populations, which is a contradiction to the expected patterns described by the Gompertz curve. He also mentions that the maximum record life expectancy has been increasing linearly during the whole 20th century and it seems it will keep increasing during part of the 21st century. These findings refuted the ideas that a human population's life expectancy at birth could not exceed a fixed figure close to 85 years, and that human beings' maximum potential life span was heavily determined by genetics.

Even though some of these results were seen initially as counter to evolutionary theory (Vaupel, 2004; Wachter,), biodemographic research was increasingly based on the theoretical framework of biological evolution. Some of the biodemographic principles outlined by Carey and Judge (2001) are based on evolutionary ideas. One of the key elements of these principles is the role of selection: "senescence is a product of natural selection on survival over reproduction" (p.12) and "selection shapes mortality trajectories" (p.17). According to evolutionary biodemographers, senescence arises from the selection of individuals who survive reproductive years thanks to their traits that make them fitter than those individuals who did not survive. The genes that help

survive reproductive age are then disproportionately distributed; however, the distributions of genes that are related to health and death in later life are still randomly distributed among survivors, explaining the increase in death rates with age (Judge and Carey, 2001). Some genes may be simultaneously related to increase survival at early ages and diminished survival at old age.

However, genetics appears to explain only a relatively small fraction of human mortality yet (around 25% to 30%). As Vaupel (2010) acknowledges, mortality postponement has been achieved thanks to medical technology, public health policies, better education and standards of living, and healthier lifestyles. Therefore, some individuals have survived to older ages not necessarily because they are less frail, but because the assistance of medical treatment. A fraction of these individuals suffered from grave diseases during childhood, adolescence, and young adulthood, but did survive to old ages. The "life course approach to epidemiology" (Kuh and Ben-Shlomo,) link bad health and other circumstances during young ages with morbidity and mortality at old ages. The "thrifty phenotype hypothesis" explains how malnutrition during gestation and infancy is a risk factor for several chronic diseases (Hale and Barker,). In their "Cancer Transition" framework, Gersten and Wilmoth () summarize the infectious etiology of several types of cancer, such as hepatic, stomach, and cervix cancer. According to Vaupel (2010), early life conditions explain just around 10% of mortality at old ages. Their computations are based on the notorious Danish Twins study. Would that proportion be the same in developing countries, where medical infrastructure and public health policies arrived later than in industrialized countries?

The Health Transition in Latin America and Costa Rica

In Europe and North America, the onset of mortality decline precedes the introduction of antibiotics and other medical technology. In his renowned hypothesis, McKeown () argues that the onset is related to an improvement in the populations' nutrition and economic well-being. In the developing countries, the introduction of this kind of health technology precedes socio-economic development. In Latin America, in particular, Palloni and colleagues (Pelaez *et al.*, 2000; Palloni *et al.*, 2002; Palloni *et al.*, 2005, 2006) have defended the notion that Latin American elderly at the beginning of the 21st century have been exposed to conditions that might lead to a higher morbidity burden in a context of rapid population aging (the aging process is occurring in less than half the time it took in industrialized countries), poverty, social inequality and weak safety net institutions. From a life course perspective, these authors argue that current elderly cohorts were exposed to malnutrition –due to pervasive poverty– and an infectious disease environment during their gestation and infancy. These conditions might increase their risk of developing certain diseases late in life: Diabetes Mellitus (according to the "thrifty phenotype" hypothesis, Hale and Barker,), cardiovascular diseases through inflammatory processes (Finch and Crimmins,), or certain types of cancer –stomach, liver, cervix– related to infections (the "Cancer Transition", Wilmoth and Gersten,). In Latin America, there is also Chagas disease, an endemic illness which can be lethal just after infection; among survivors, Chagas disease can remain latent and evolve into congestive heart disease several years after infection.

The situation is Costa Rican elderly is very similar, although Costa Rica is an exceptional case in terms of mortality decline and the institutional context of health services. Historical records show that mortality started to fall slightly during the second part of the 19th century after a severe cholera epidemic during 1856 that might have killed near 1/15 of the country's total population (Lachner, 1902). After this epidemic, Costa Rica was favored by a low population density and a slight improvement in socio-economic conditions due to coffee exports. According to Rosero-Bixby (1984), a sharp fall in death rates occurred during the period 1920-1960, but especially after 1945, due to the creation of public health institutions (the Ministry of Health, the Social Security Fund) which organized preventive and primary care services, and the import of medical sanitary conditions, such as antibiotics, DDT, and vaccines. Life expectancy at birth increased from 35 years in the 1920s to 63 years at the end of the 1950s. This mortality trend slowed down during the 1960s decade, but declined fast again after 1970. This decline is related to the Rural Health and Community Health programmes that expanded the access to primary health care services in underserved areas, the expansion of Social Security (which encompasses retirement and health insurance) to rural workers and socio-economically disadvantaged groups, an expansion of the provision of drinking water and sewage systems, and the institutionalization and modernization of vaccination to infants. There was also an improvement in living conditions due to the post-war economic growth, clearly illustrated by the improvement of communication infrastructure and education (Rosero-Bixby,). Finally, during the last decade of the 20th century and the first decade of the 21st century, Costa Rica underwent a Health Care reform, promoted by the Government, the World Health Organization and the World Bank. Among the highlights of this reform, there was a rationalization of health care costs. This was achieved by giving the administration of all health care services to the Social Security Fund (some of them were managed by the Ministry of Health), which in turn decentralized the administration to Regional Offices within its organization. A very successful policy was the creation of EBAIS, primary health care teams made up of health care professionals (physicians, nurses, and community health workers, and in some cases pharmaceutics and microbiologists) who work in both urban and rural areas. Rosero-Bixby (2004) shows that the introduction of EBAIS is associated with infant mortality declines during the 20th century late years.

Nowadays, life expectancy at birth in Costa Rica is 79.3 years (76.8 for men and 81.8 for women) (INEC, 2010). Life expectancy at age 60 is 21.98 for males and 24.88 for females. People aged 60 and over represent 9.3% of the total population in 2009 (INEC/CCP, 2009). Costa Rican elderly people are characterized by having a very high coverage of health insurance (94%), a relatively high proportion receiving retirement pension (40%) or public subsidies (14%) from the government compared to other Latin American countries (own computations, based on CRELES data), and a higher prevalence of poverty when compared to the non-elderly population (Fernandez and Robles, 2008). Besides, Costa Rican elderly have contradictory SES health gradients: while higher SES elderly are better off in self-rated health, disability status, and depression, they are worse off in mortality and in the prevalence of hypertension and obesity (Rosero-Bixby and Dow, 2009).

Even though Costa Rican elderly have advantages in terms of access to health care and life expectancy, they were all born during the first half of the 20th century, before the great improvements in health explained above. Infectious diseases were highly prevalent during these cohorts' early years. In 1930, malaria, diarrhea, and intestinal parasitic illnesses accounted for

36% of all deaths. These causes of deaths were virtually eradicated since the 1940s. Rosero-Bixby (1984) estimated that 18% of the total mortality decline from 1940 to 1980 can be attributed to the decrease in malaria mortality. The reduction in malaria deaths was achieved after the introduction of insecticides after World War II. Therefore, it can be expected that a non-negligible proportion of the elderly population have at some point contracted malaria. The actual figures according to our data will be shown in the results section.

Cerebral malaria and cerebrovascular accidents

Data and Methods

Data

We use the dataset from CRELES, the "Costa Rican Study on Longevity and Healthy Aging". It is an on-going longitudinal study of a nationally representative sample of 2,827 adults born in 1945 or before (ages 60 and over at the first interview) and residing in Costa Rica by the year 2000. CRELES was funded by a Wellcome Trust grant and has been approved by the Institutional Review Board (Comité de Ética) of the University of Costa Rica. Its protocol has also been reviewed by the IRBs of the University of California-Berkeley and the University of Wisconsin-Madison in order to let researchers participate in the project.

The first wave of interviews was conducted from November 2004 through August 2006. The second wave started in November of 2006 and concluded in July 2008, and the third wave was conducted from October 2008 through December 2009. All data and specimens in the study were collected at the participants' homes, usually over two visits. In the first visit, participants provided informed consent for the interview and answered a 90-minute long questionnaire (including some mobility tests and two blood-pressure measures) as well as a 10-minute frequency of tracer food consumption questionnaire. In a second visit early the next day, fieldworkers collected anthropometric measures, and urine and fasting blood samples (the procedures followed for storing and processing the specimens are described in Mendez-Chacon *et al.*, 2007). All field data were collected using Personal Digital Assistants (PDAs), with software applications developed by Centro Centroamericano de Poblacion (CCP) for this study.

CRELES has a complex sampling design. There is an original master sample of 9,600 individuals that was randomly selected from the 2000 census database with stratification by 5-year age groups and over sampling of older individuals. Within each stratum, persons were selected using simple random sampling involving a systematic selection procedure. In the master sample, sampling fractions ranged from 1.1% among those born in 1941-45 to 100% for those born before 1905. The individuals in the master sample were grouped into 102 geographical clusters according to the 102 "Health Areas" created by the Government. The final sample for the in-depth interview is composed of a probabilistic sub-sample of clusters: 60 "Health Areas" (out of a total of 102). This sub-sample originally included nearly 5,000 individuals and covered 59% of Costa Rican territory. The first wave fieldwork yielded the

following non-response rates: 19% deceased by the contact date; among those alive, 18% were not found in the field, 2% moved to other addresses, 2% rejected the interview, and 2% pendant interviews after several visits (likely rejections). After non-response, the resulting sample size for the first wave amounts to 2,827 individuals. The final sample size for the second wave totals 2,364, which is equivalent to a 16% attrition rate: 10% deceased by the contact date and 6% that could not be located or refused to answer the interview. The final sample size for the third wave is equal to 1855 respondents. The attrition rate with respect to 22%: 12% deceased and 10% due to refusal or problems to locate them. Final sampling weights are computed as the inverse of selection probabilities, which take into account the complex sampling design (selection of the master sample and of the second sub-sample), as well as differential non-response rates. All statistical analyses take sampling weights into account.

Furthermore, 703 persons in the first wave, 676 in the second wave, and 478 in the third wave needed a proxy respondent to answer the survey questions. This information is important to highlight because the question used to construct the main independent variable (having had malaria before age 15) was asked only to respondents who did not need a proxy.

The main dependent variable is death. CRELES has two ways of verifying death. The first way is a linkage with the Costa Rican Death Index (Registro de Defunciones). The linkage is made using the Costa Rican national id number. The Costa Rican Death Index has a very high coverage (INEC/CCCP, 2009). Its main problem is late registration, given that around 3% to 4% of deaths are entered into the Death Index Database within 2 years of its occurrence. In order to avoid biases in our linkage, we censored our observations around 1.5 years before the closing date of the Death Registry that we request. The other way of obtaining the date of death is through the decedent questionnaire interview. If a respondent is deceased by wave 2 or wave 3, the fieldworkers interview a relative or close acquaintance of the former respondent about the circumstances of the death: 514 deaths were found through the decedent questionnaire and 85 additional deaths were found through the data linkage. Almost all deaths registered during fieldwork were verified through the data linkage (Luis Rosero-Bixby, the project PI found 3 cases that were not still registered in the Death Index, but were found dead during fieldwork). Preliminary results about the cause of death are derived from the decedent questionnaire. The cause of death will be verified through a special linkage to the Death Index that has the ICD-10 codes.

As mentioned before, the main independent variable is having had malaria before age 15. This variable is drawn from self-reports to a question in the first wave: “Did you have malaria during childhood or adolescence?” This question is only asked to non-proxy respondents. A more thorough question about malaria during adulthood was included in the second and third wave questionnaires. However, the time period since the second wave is still too short to have enough decedents for a survival model. We acknowledge that this question might have reporting errors. However, malaria is a disease that is so harsh in its effects and that was pervasive enough during the first half of the 20th century in Costa Rica to be remembered.

Methods.

We use inferential tests of differences of means and differences of proportions in order to assess how different (or select) are the malaria survivors with respect to the rest of the Costa Rican elderly population. We test differences in proportions across sex, place of residence, education, living alone status, income, self-reported financial situation, health insurance, public subsidies, and baseline prevalence of hypertension, hypercholesterolemia, diabetes mellitus, lung disease, heart attack, cancer, osteoporosis, arthritis, and geriatric falls. We also perform t-tests for differences in age and hand grip strength (in first wave). T-tests for differences in mean levels of several biomarkers (triglycerides, glycated hemoglobin, low-density lipoprotein, and glucose) are estimated but are not shown in tables because they agree with previous tables.

We then estimate competing risks Gompertz survival models to estimate the relative risks (or hazard ratios) of dying due to stroke, other cardiac diseases, non-defined causes, and other causes, of malaria survivors compared to the rest of the Costa Rican elderly populations. First, we estimate simple models, with the main independent variable. Second, we estimate a complex model that controls for

Results

Among Costa Ricans born before 1945 and alive in 2004, 11% reported that they had malaria before age 15. The older cohorts were more likely to report the disease (Figure 1): malaria prevalence was around 15% among people born before 1935, and it decreased 8% among the youngest cohorts. This cohort trend suggests that there were more effective sanitary measures to prevent malaria infections put in place during the second quarter of the 20th century. CRELES did not ask for infections after age 15 during the first wave; it did during the second wave and third wave. Among the people interviewed in the second wave, 9% reported having been ill due to malaria before age 15, 4% between age 15 and age 29, and 1.4% after age 30. Rather than differential exposure across ages, this trend reinforces the idea that there was better sanitary control against malaria during the second part of the 20th century.

There were several socio-demographic differences between malaria survivors and the rest of the Costa Rican elderly (Table 1). Malaria survivors were on average older, and predominantly males, less educated, and living outside the Central Region. They also fared worse in SES indicators: they were more likely to earn less than 50,000 colones (aprox. US$100) per month, to report fair or bad financial situation, and to receive public subsidies aimed at poor elderly (called "non-contribution pensions). We expected these differences in the analysis because they clearly show which population groups were more exposed to malaria: males, people living in lowlands, and people with low SES. However, it is worth noticing that there were no differences in the prevalence of not having health insurance. This figure is important because it shows that there was relatively equitable access to health insurance among Costa Rican elderly, regardless of SES.

A key point in the analysis is assessing health differentials between malaria survivors and the rest of the population (Table 2). The former were more likely to qualify their health as fair or bad. However, there were no significant differences in the prevalence of diseases, including conditions that are known risk factors of stroke: hypertension, hypercholesterolemia, diabetes mellitus, and heart attacks. No significant differences were found in levels of biomarkers

associated with vascular diseases (not shown in Table): plasma glucose, triglycerides, glycated hemoglobin (HbA_{1C}), and High Density Lipoprotein (HDL). The only significant difference in disease prevalence was in cancer: 9% of malaria survivors reported to have a physician diagnosis of cancer, while only 5% of the non-malaria population reported to have it. Both malaria survivors and people with no early malaria history had similar mean hand grip strength and similar proportions with ADL limitation, but the former were more likely to report having IADL limitations. Additionally, there were no significant differences in alcohol drinking prevalence or in obesity, but malaria survivors were more likely to be former or active smokers (53% vs. 42%). Smoking is also a risk factor of stroke. Malaria survivors were also more likely to report typical early symptoms of vascular disease, such as dizziness and fatigue (but not nausea).

What do these results show within an evolutionary biodemographic framework? Malaria survivors were neither frailer nor healthier than people with no malaria history; they just seemed to have a very similar health profile to the rest of the population. Therefore, they did not seem to be a selected group, except in the prevalence of cancer, IADL limitations, and smoking history, where they fared worse than their counterparts. However, based on the cross-sectional data of the first wave, they did show early symptoms of stroke, such as dizziness and fatigue.

In wave 1, stroke prevalence was 2.3% among respondents. Prevalence among malaria survivors was 3.7%, while among people who did not have the disease, the prevalence was 2.2%. This difference was not significant at a 5% level. The difference in the probability of having a stroke between wave 1 and wave 2 (3.2% vs. 1.5%) was only significant at a 10% level. Death rates due to stroke (6.3 per 1000 vs 0.5 per 1000) were significantly different. These results suggest that the lethality of cerebrovascular accidents seemed to be higher among malaria survivors.

We estimated a set of competing risks Gompertz regressions (Table 4) in order to assess whether this difference in death rates was spurious, after controlling for other covariates, especially those that are related theoretically to stroke mortality and that were associated with having an early life malaria history. The set of equations compares mortality due to stroke, to cardiac diseases, to non-defined causes, and to other causes. The first set of models –called simple equation– had the binary variable malaria as the sole covariate; the complex equation controls for the covariates shown in Tables 1 and 2, except self-reported symptoms (dizziness, fatigue, and nausea). The relative risk of dying due to stroke among malaria survivors compared to the rest of the population was 11; this figure increased to 15.7 after controlling for confounders. The Gompertz coefficient in both stroke equations was significantly different to zero. The hazard ratios for the other causes of death were not significantly different to one. These results were robust to distributional specifications (exponential, weibull, log normal, log-logistic, semi-parametric Cox models) as well as to the Gompertz model accounting for frailty (gamma distribution).

It is also worth noticing that the other covariates with significant effects on stroke mortality were: diabetes mellitus, cancer, and lung disease. The increase in the size of the hazard ratio for having malaria seemed to be independent of the prevalence of other risk factors of cerebrovascular disease.

Discussion

References.

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Figure 1. Costa Rica: Percentage reporting malaria before age 15 among people aged 60 and over in 2004, by cohort (Weighted data).

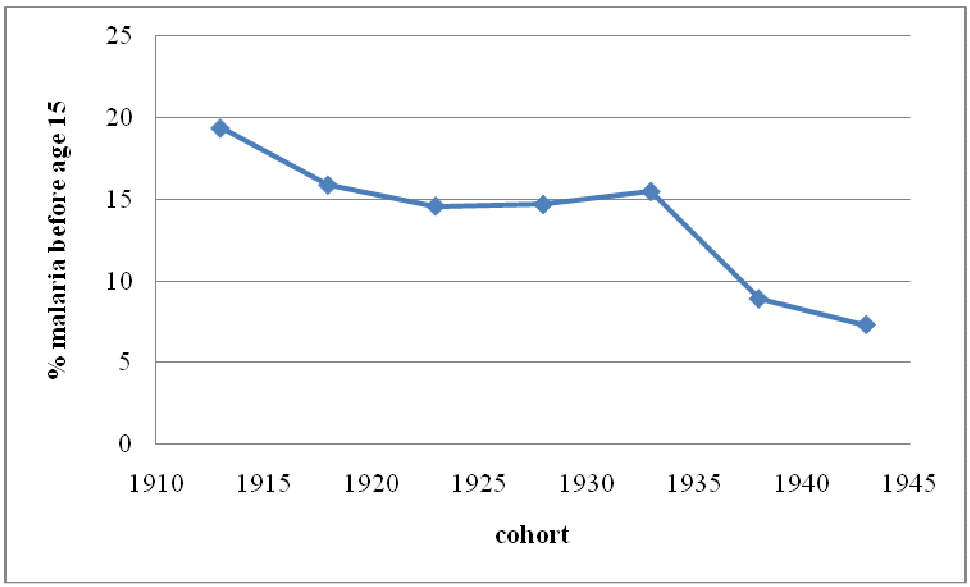


Table 1. Costa Rica: Baseline socio-demographic characteristics among people aged 60 and over in 2004, by reports of malaria at early age (before age 15). (Weighted data).

Socio-demographic characteristics	Self-reported	malaria before age 15	Test of differences (p-value)
	Yes	No	

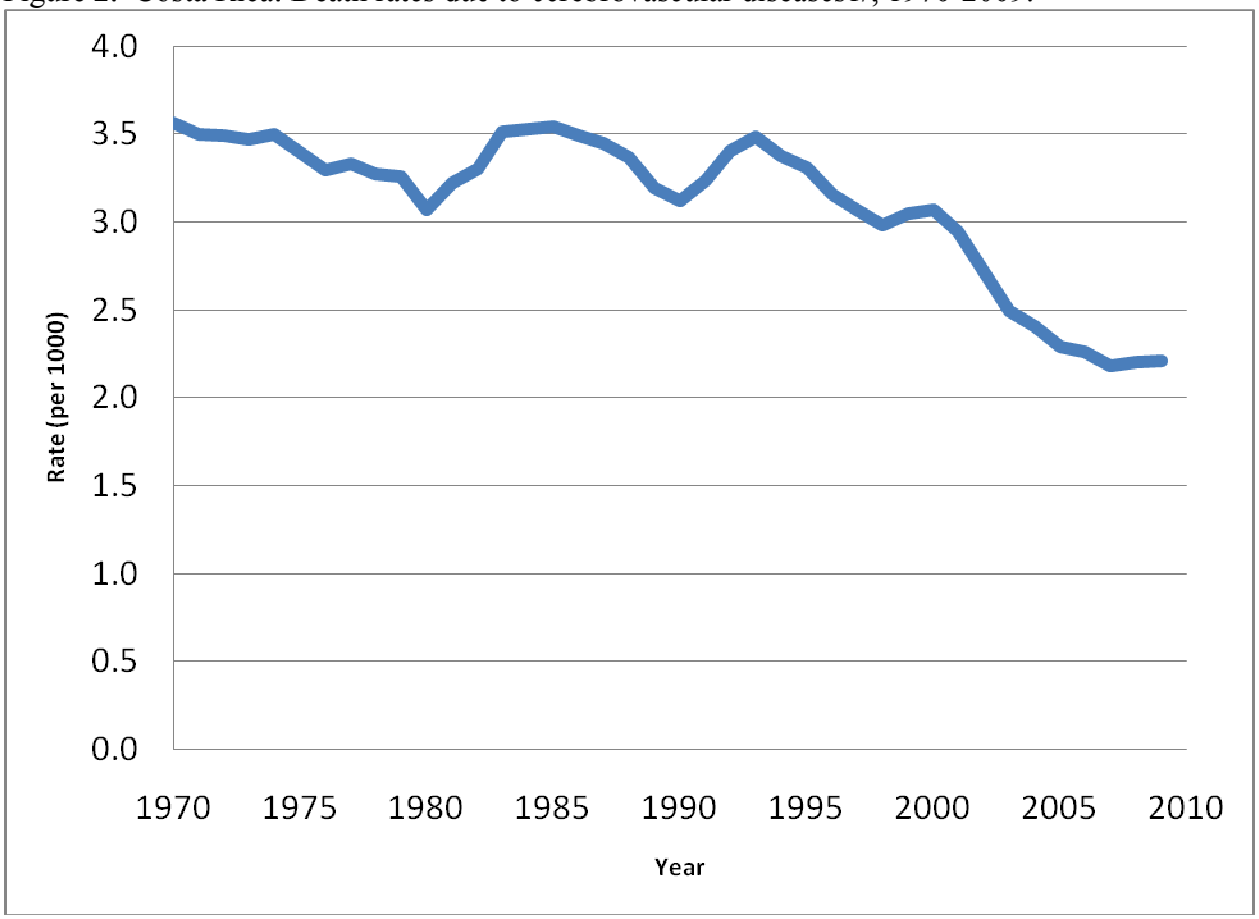
Mean age (sd)	71.4 (7.1)	68.9 (7.0)	0.000
% females	42	53	0.005
% with 6 years of formal education or more	40	55	0.000
% living in Central Region (Great San Jose)	29	56	0.000
% with couple's income <50000 colones (aprox.US$100) per month	45	37	0.028
% reporting fair/bad financial situation	67	55	0.003
% no health insurance	4	4	0.635
% with public subsidy for the poor	19	11	0.000
% living alone	12	10	0.312
% neither married nor in union	37	37	0.987

Table 2. Costa Rica: Baseline health characteristics among people aged 60 and over in 2004, by reports of malaria at early age (before age 15). (Weighted data and standardized by age, sex, place of residence, education, living alone status, income, report of bad financial situation, no health insurance, and public subsidy for the poor).

Baseline health characteristics	Self-reported malaria before age 15		Test of differences (p-value)[1/]
	Yes	No	
% reporting fair/bad health	61	43	0.000
Prevalence (%) of:			
-Hypertension	47	48	0.768
-Hypercholesterolemia	41	41	0.875
-Diabetes mellitus	19	21	0.495
-Lung disease	17	16	0.769
-Heart attack	6	4	0.266
-Cancer	9	5	0.007
-Osteoporosis	12	9	0.136
-Arthritis	19	14	0.075
-Geriatric Falls	41	34	0.066
% currently smoking	12	10	0.036[2/]
% smoker before	41	32	
% currently drinking alcohol	32	36	0.544[2/]
% drinking alcohol before	33	30	
% obese	25	28	0.511
Mean hand grip strength in Kg (sd)	27.7 (8.9)	27.8 (8.9)	0.917
% with at least one ADL limitation	66	61	0.124
% with at least one IADL limitation	18	12	0.008
Self-report (%) of:			
-dizziness	39	30	0.008
-fatigue	41	31	0.003
-nausea	11	7	0.138

Notes: 1/ Pearson X^2 for proportions, and t-test for means.
2/ The Pearson X^2 test is computed for the whole categorical variable related to smoking or alcohol drinking rather than separately to each dichotomous variable.

Figure 2. Costa Rica: Death rates due to cerebrovascular diseases1/, 1970-2009.



Source: Figures processed from Costa Rica's Death Registry and Population Projections, INEC/CCP, at: http://censos.ccp.ucr.ac.cr/.

Notes:	ICD codes: 430-439 in ICD-8 and ICD-9, and I60.0 – I69.9 in ICD-10

Table 3. Costa Rica: Stroke prevalence and incidence (2004-2009) among people aged 60 and over in 2004, by reports of malaria at early age (before age 15). (Weighted data).

Self-reported malaria before age 15	(n)	Stroke prevalence in wave 1	Stroke incidence wave 1-wave 3 (including mortality by stroke)[1/]	Death rate due to stroke (no multiplier)
		(%)	(%)	
Yes	279	3.7	3.2	0.00628
No	1824	2.2	1.5	0.00053
Total	2103	2.3	1.7	0.00118
Test of differences (p-value)		0.18[2/]	0.091[2/]	0.000[3/]

Notes: 1/Stroke incidence is computed as the proportion that reported or died of a stroke between wave 1 and wave 3, from main or decedent questionnaire.
2/ Pearson X2 test p-value
3/ Mantel-Haenszel test p-value

Table 4. Costa Rica: Coefficients for having had malaria before age 15 (self-reported at baseline) in competing-risks Gompertz regressions of dying due to stroke, cardiac diseases, non-defined causes, and other causes. Simple and complex equations. CRELES project. (Weighted data).

Competing risks-	Simple equation			Complex equation [1/]		
mortality equations	Coeff	Hazard ratio	p-value	Coeff	Hazard ratio	p-value
For self-reported malaria						
Stroke	2.40	10.97	0.007	2.76	15.74	0.007
Cardiac diseases	0.22	1.25	0.609	0.03	1.03	0.953
Non-defined causes	-0.19	0.83	0.654	0.03	1.03	0.947
Other causes	0.31	1.36	0.308	0.15	1.16	0.665

Note: 1/ The complex equation includes the following covariates: sex, place of residence, education, living alone status, income, self-reported financial situation, health insurance, public subsidies, and baseline prevalence of hypertension, hypercholesterolemia, diabetes mellitus, lung disease, heart attack, cancer, osteoporosis, arthritis, and geriatric falls.