UNIVERSIDAD DE COSTA RICA

CRELES Pre-1945

Costa Rican Longevity and Healthy Aging Study Methods, Wave 1

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DATA AND METHODS

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This report presents the information of the first round of the research project "Costa Rica: A Study of Longevity and Healthy Aging (CRELES)". The study is conducted by the Central American Center of Population (CCP) of the University of Costa Rica, with the collaboration of the Institute for Health Research (INISA) of this university and other public entities such as the Costa Rican Office of Social Security (CCSS) the National Council of Senior Citizens (CONAPAM). The study has received funding from the Wellcome Trust Foundation.

CRELES is a longitudinal type of study based on a national sample representing older adults in Costa Rica, with a subsample oversampling of older seniors. The criteria for inclusion in the study is that the persons be residing in Costa Rica, disregarding for their nationality, and to have been born before 1946, that is, 60 years of age or older at the time of the first interview.

For the present analysis, the data of the first round of interviews are used, carried out between November of 2004 and September of 2006. The size of the sample is of about 3,000 interviewed people.

Design of the sample

In the first stage of the design model, a random selection was made from the database of the Census of Population of the 2000, totaling 9,600 individuals 55 years of age of older, after a stratification by five-year age groups that assures a sufficiently large number of observations for advanced ages. The sampling fraction in this selection varies between 1% for the ones born in 1941-1945 and 100% for the born ones before 1905. For the detailed longitudinal follow-up, including the survey to which the present report refers, a sub-sampling was selected consisting of 60 "Areas of Health" (from a total of 102 in the whole country) aggregated into sub-regions. The sample covers 59% of the national territory. The map in figure 1 shows the zones in the country included in CRELES and the location of the participants.

The sub-sampling for the longitudinal study originally included near 5,000 individuals from the census of 2000; of those, it was possible to locate and to interview to 2,827. The no-answer rates are comprise of: 19% of deceased by date of contact, 18% of people were not located in the field, (due mainly to the lack of accurate addresses), 2% had changed residence, 2% declined to be interviewed and 2% of interviews were pending after several visits (that in fact are veiled rejections). Among the interviewees, 95% provided blood samples, 92% urine samples; 91% was able to apply the anthropometry module and 25% required a "proxy" who could respond to the questionnaire.

The 20% no-response for change of residence or not-located is concentrated among the younger ages and it is different by city and social condition. To correct this distortion and to take into account the different sample fractions by age, a series of counter weights were determined by age, sex, urban residence and two education groups (schooling less than 6 years and schooling 6 years or more). These weights allow the replication of the structure for sex, age, residence and education of the whole 2005 population of Costa Rica born in 1945 or before. The weights were also normalized so they reproduce the sample size of 2,827. These weights varied from minimum of 0.07 for men 95 years of age and older with low education, to a maximum of 3.85 for men age 60-64, high education and rural residence. All the results of this report are weighted so they represent the average for the subject population.

Graph 1. Map of the health areas of Costa Rica and the interviewees in CRELES

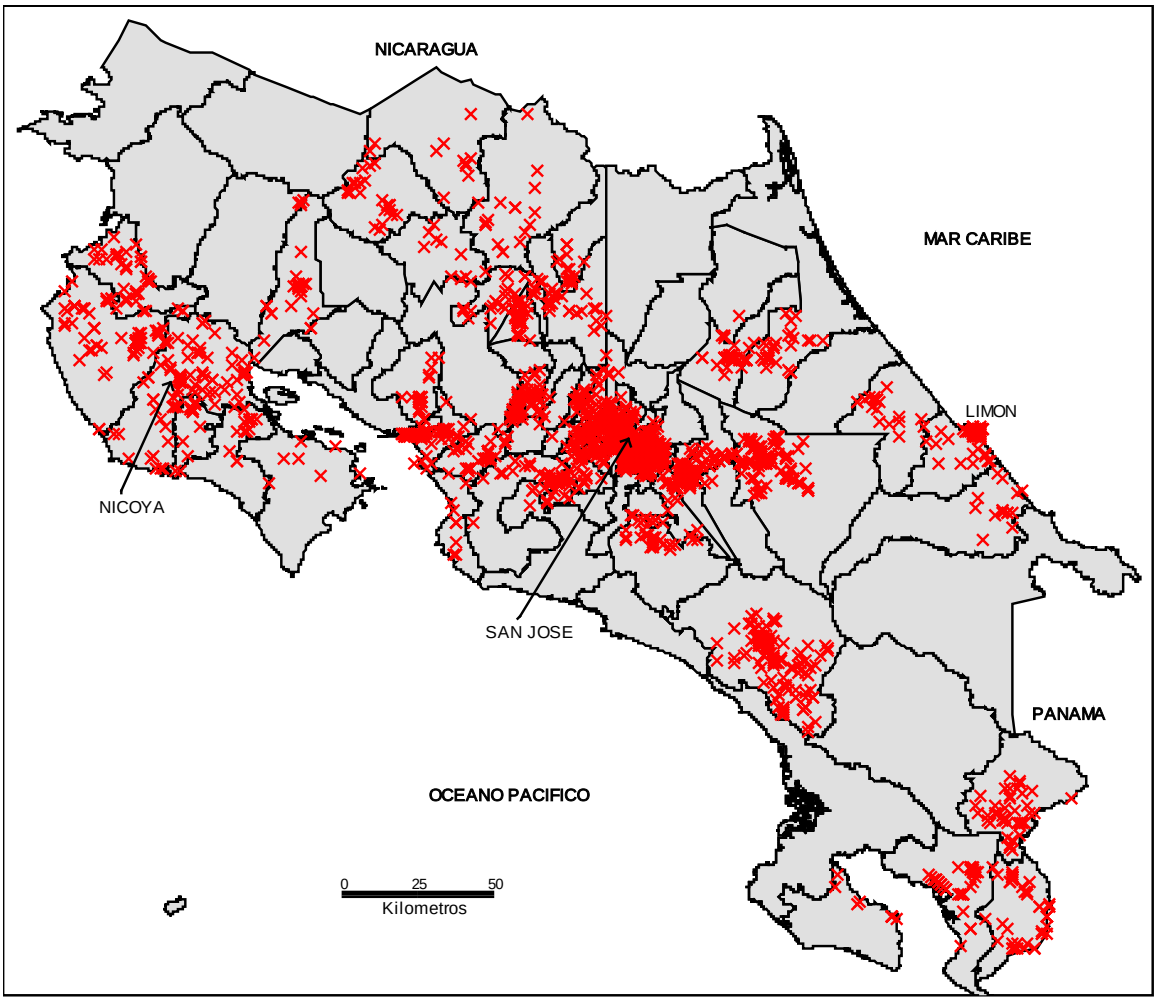

Table 1 compares selected data of this study with the Survey of Homes with Multiple Purposes (EHPM) of Costa Rica of Julio 2005, an annual research effort conducted by the National Institute of Statistics and Censuses (INEC) in a national sample representing more than 12,000 homes. A good amount of coherence was applied between both research works, which suggests the absence of biases that could have damaged the representativeness of the sample. Differences of up to 4 percentage points may well be due to the random selection since they are comparing two different samples of the same population. The only important difference is in the percentage of heads of households: 66% in CRELES compared to 60% in the survey of homes. However this difference is explained because in CRELES the informant is the same older person while in EHPM it can be another person with a different perception on who is the head of the household.

Table 1: Comparison with data of INEC, Survey of Household of Multiple Purposes 2005. (Population of 60 and more years of age)

Indicator	CRELES		EHPM
	Observed	Weighted	2005
(N)	(2.827)	(2.827)	(3.834)
Index of masculinity	84.3	90.3	88.3
Average age	76.4	70.4	70.9
% secondary education or +	14.1	21.8	23.1
% in urban area	60.1	62.6	62.2
% in homes 1 or 2 members	41.0	38.5	39.6
% head of household	61.5	65.7	60.4
% married	49.7	60.3	57.2
% widowers	32.2	21.4	22.6
% economically active	20.3	29.4	26.2

EHPM = Survey of Homes of INEC, source database in Internet

Field Work

The study, being longitudinal, consists of ate least two rounds of visits separated by two years. This report presents the results of the first round, in which a structured interview was conducted, anthropometric measurements were taken, physical functionality tests were given and blood and urine samples were taken. All the data and specimens were gathered in the homes of the participants, generally in two visits. In the first visit, the participants granted their informed consent (Appendix 1) by means of their signature, and they answered a questionnaire of around 90 minutes which includes two readings of arterial pressure and a series of questions (lasting 10 minutes) on food consumption. In the second visit to the participant's home, early the following day, the blood samples were taken while fasting, the urine sample received was collected at night, and the anthropometric measurements were taken and the physical functionality tests were given, including hand-strength and maximum peak of breathing flow.

At the beginning of the interview a cognitive evaluation was included that, together with the interviewer's criteria, establishes the need for, or not, an informant or "Proxy" for the participant to help to respond the questions. Of the interviews, 25% were conducted with the help of a Proxy.

All the data of the fieldwork were registered using handheld computers or "Personal Digital Assistants" (PDAs), also known as "Palms", with a software application developed in CCP for this study. The main questionnaire, that is very complex, was programmed into the Palms. Appendix 2 includes a hard copy version of the main questionnaire, as well as the diet and anthropometry, programmed into the Palms. It should be noted that in the pilot study of the questionnaire the answers were registered in the Palm and on paper at the same time, assuring a good level of dependability (Hidalgo-grass, Rosero-Bixby et al. 2007). The Palm shows on the screen the text of each question that the interviewer should read and, when needed, it also provides instructions. The answers are usually register in the Palm pressing on the screen ("tapping") on the selected option from a list, but also it can be registered by entering numbers or text directly in "graffiti" or, if so choosing, into a virtual keyboard. The Palm controls the flow of the interview; that is to say, it skips questions and employs filters based on

previous questions. It also executes verifications of consistency programmed ahead of time, and it automatically generates certain variables as the date and the hour. The Palm doesn't allow registering of inconsistent data or date outside of the range, nor does it allow to skip the sequence of questions. The data are thus ready for the analysis in the computer at the moment that the interview is completed. The Palms also included ahead of time the information on the summary areas, particularly all the pre-known information of the geographical identification and of the individual. This information automatically moved to each interview with the concomitant time-saving and elimination of transcription and identification errors.

Also registered in the field were the data of the geographical coordinates of the place of each participant's residence, using GPS devices.

The fieldwork to gather the information of the first round was conduct from November 2004 to September 2006; that is to say, during a period of 22 months. A team of 5 interviewers with a supervisor took charge of locating the subjects in the sample, processing the informed consent an conducting the main interview as well as the diet interview. The team conducted an average of 7 interviews per day. Another team comprised of two phlebotomists and an interviewer of the first team obtained the samples of blood while fasting, it gathered the urine sample of 12 hours and it took the anthropometrics measurements (body weight, height, height of the knee, abdominal circumference, circumference of the hip, circumference of the calf, circumference of the arm, tricipital and subescapular skin-fold measurements), and physical functionality test. The interviewer in this team had been ahead with the other team and served as guide to locate the interviewees. The entire data collection was carried out in the home of the participants.

Physical, anthropometric and mobility and flexibility tests:

The following describes materials, equipment and methods used in the physical exams used on the senior adults of the study: blood pressure, anthropometric measurements, flexibility and mobility tests, hand strength and peak breathing flow. More detail of the tests is available in the interviewer's manuals on the project website: (http://ccp.ucr.ac.cr/creles/index.htm).

Blood pressure

It was measured on two occasions during the general interview, with an average interval time of 20 minutes between each; the measurement was taken using OMRON brand digital monitors with automatic inflating, model HEM-711AC, DuPont (precision: ± 3mmHg) that were calibrated periodically. The bracelet was adjusted to the thickness of the adult's arm.

The anthropometric measurements

They were taken by the interviewers who were trained and certified for this purpose, with updated training after a year of fieldwork. The measurements taken and the equipment used are the following:

Body weight: The scale used was the Life Source brand, M&D medical, model UC-321p; it was placed on even floor and without carpets, the measurement was carried out without shoes, nor objects of weight in the pockets of those participants with clothes.

Height: A Seca brand stadiometer was used to measure the height of the senior adults. The measurement was not taken if the person had major deformations of the spine.

Height of the knee: The measurement was carried out in the right leg whenever the interviewee did not have a present a lesion on it. For this measurement a (Goniometer or Inclinometer?) to indicate the angle of 90 degrees, and then it was measured with a stadiometer manufactured by Shorr Productions a Maryland company, called Shorr USES Knee-Height Caliper.

Abdominal measurement and Circumference of the hip: These measurements were made with the participants standing, in a semi-anatomical position (with the feet separated and the palm of the hands resting on the lateral thigh). The metric tapes used were the Dry and the Quick Medical brand tapes.
Circumference of the calf: In this case the person should be seated, with the right leg exposed.
Circumference of the arm: With the person seated or standing, the circumference was measured in the half point between the acromion (or posterior bone of the shoulder) and the olecranon or protruding bone of the elbow.

Tricipital and sub-scapular skin folds: The interviewer carried out the measurements using his thumbs and index fingers in order to make sure to only take the fatty tissue and not muscles or nerves. For this, a Lange Skinfold caliper, from Beta Technology Incorporated, was used.
Hand strength: Two measurements of hand strength were taken (the highest value is used in the analysis) with the interviewee standing with the dominant arm extended beside their body. A Creative Health Products Inc. dynamometer of was used, model T -18.

Peak breathing flow or lung function. The maximum respiratory volume was measured in liters per minute with Mini-Wright type meters. These are homologated meters; that is to say, they have an acceptable correlation with the following: vitalograph, Sibelmed, PF - control, Clement Clark, Asses and TruZone. Three consecutive measurements of peak flow were taken.

Flexibility and mobility

The flexibility and mobility tests were carried out with the purpose of measuring (1) equilibrium and balance, (2) agility and (3) walking speed. The exercises that were carried out were the following:

Equilibrium and balance: To measure equilibrium and balance two tests conducted (1) to remain standing with feet together for 10 seconds and (2) to stand up five times from a sitting position, with arms crossed on the chest.

Agility: The agility was measured to beginning with the senior's ability to bend over, to pick up a pencil and to straighten out. If the interviewee could not do it in less than 30 seconds the test was not continued. The test was also not conducted if the senior had a cataract operation or another retinal procedure in the six weeks previous to the test.

Walking speed: To measure the senior's ability to rise off of a chair and walk, the interviewee was asked rise from a chair and walk a distance of 3 meters in the manner that he normally does it; neither slower nor faster. The test was registered with a chronometer, noting the time in seconds that it took to carry out the test.

Laboratory procedures

The blood sample was obtained by venipuncture, normally during the second visit, the day after the main interview, with the participant fasting (for 14 hours). Three tubes of blood samples were collected: One with anticoagulant (VACUTAINER / EDTA) of 3-4 ml that was centrifuged later to separate the plasma of the cells and two tubes without anticoagulant with coagulum activator (VACUTAINER SST, 5 ml) for obtaining serum. In the laboratory a fraction of serum was separated in a tube conical tube type Eppendorf for total cholesterol tests, HDL, LDL, triglycerides, glucose, and serum creatine and 1 ml of complete blood in the tube EDTA for the analysis of glycosylated hemoglobin. These tubes were sent immediately to the participant laboratories for analysis. The remaining fractions of serum and plasma were aliquoted in red-top cryovials and they were stored in ultra-refrigeration (-140°C). In this visit, the interviewers also gathered an ice box with a 12-hour sample of urine taken during the night, which was maintained cold with ice gel, and they took anthropometric

measurements. After measuring the volume of the urine sample a fraction it was stored in aliquot at -40°C. In the field, in areas far from San José the project had the cooperation of laboratory units of the CCSS that provided the space for the initial preparation of the blood and urine samples.

The biomarkers measured starting from blood and urine samples of the CRELES Project were analyzed in different laboratories. The clinical chemistry tests were made in the Clinical Chemistry laboratory of the Department of Clinical Analysis of the College of Microbiology of the University of Costa Rica and in the clinical laboratory of the Hospital San Juan de Dios (HSJD). The measurement of the Glycosylated Hemoglobin was carried out in the above-mentioned laboratories using automated methods and also in the clinical laboratory of the Office of Health and Student Well-being of the University of Costa Rica (UCR).

Table 2 shows the techniques used in the different laboratory tests and quality control. The variability among laboratories was also evaluated with comparisons between batches of 20 samples taken at random and without the laboratories knowing that this comparison was being conducted (Méndez-Chacón, Rosero-Bixby et al 2007). In all the cases, high correlations were found among the series from different laboratories, but for some markers there were some systematic differences that were detected. To eliminate these differences one of the laboratories was established as the standard (Laboratory of the Hospital San Juan of God with automated technology) and the results of the others were adjusted with equations estimated by regression in the validation batches. Chart 3 presents the correction equations that were used.

The Laboratory of the Neuro-sciences Research Program (PIN) of UCR analyzed the urine samples to determine Epinephrine and Norepinephrine. The high yield liquid Chromatography (HPLC) technique was used. Modifications to the protocol of the kit of the commercial firm Bioanalytical Systems were carried out since it did not produce the expected results in the solid phase extraction. The modifications consisted of decreasing of the elusion speed (0.1ml/min) and the quantity of the collected eluent (0.5ml), also modified was the injection flow (1.5ml min), the temperature of the analytic column (28°C) and the intensity of the applied current (10nA in the first 15 min and 20nA in the subsequent time). Both were adjusted by urinary creatinine.

Cortisol and the DHEA-S were determined by an automated process of chemiluminescence using an IMMULITE in the laboratory of the Central American Center of Hormonal Analysis (Cenahce. Ltda). The cortisol was adjusted by urine volume and urinary creatinine.

Reactive protein C was determined in the laboratory of the Central American Center of Hormonal Analysis (Cenahce. Ltda) and in the laboratory of the Hospital San Juan de Dios (HSJD). In the first laboratory the "PCR of high sensibility" method was used with the automated equipment KONELAB TM and in HSJD they used the aggregation of particles covered with monoclonal anti PCR antibodies and the Dade Bohering BN System automated equipment. The HSJD was established as the standard laboratory and the Cenahce Ltda. results were adjusted, starting from an equation estimated by regression in a validation lot.

Table 2: Analytic methodologies used by each laboratory.

Analysis	[1]Laboratory A	[2,3]Laboratory B	[4]Laboratory C	[5]Laboratory D
Glucose	Enzymatic	Enzymatic	Enzymatic	N/A
Cholesterol total	Enzymatic	Enzymatic	Enzymatic	N/A
HDL-Cholesterol	Precipitation y determination enzymatic	Method direct	Method homogeneous	N/A
Triglycerides	Enzymatic	Enzymatic	Enzymatic	N/A
Creatinine (serum & urine)	Jaffé Reaction	Jaffé Reaction	Jaffé Reaction	N/A
Glycosylated Hemoglobin	N/A	High yield Liquid Chromatography of (HPLC)	Inhibition with latex agglutination	Turbidimetric Immunoinhibition
Internal quality control	Daily Control of two levels, equipment calibration	Daily Control of two levels, equipment calibration	Daily Control of two levels, equipment calibration	Daily Control of two levels, equipment calibration
External control of quality	A. Quality Assurance Program (INCIENSA) B. External Quality Evaluation Program (PEEC) of the School of Microbiologists and Clinical Chemicals, CR	A. Beckman NYSSTATH Programs B. External Quality Evaluation of Lipids and Glucose Program (INCIENSA) C. BIORAD in England (for glycosylated Hemoglobin)	A. External Quality Evaluation of Lipids and Glucose Program (INCIENSA)) B. External Quality Evaluation Program (PEEC) of the School of Microbiologists and Clinical Chemicals, CR	RIQAS-England (Randox International Quality Assessment Scheme) for glycosylated hemoglobin

[1] Manual method, FOB WIENNER
[2] Automated Method, SYNCHRON CX7
[3] Automated Method, BIORAD Variant II hemoglobin A1C
[4] Automated Method, ACE Alpha Wassermann
[5] Automated Method, TUB QUANT

Table 1: Corrections to standardize laboratory results.

Biomarker	Lab. A.	Lab. C.	Lab. E.
Glucose mg/dl	*-20.204 +1.2218*x*	*6.687 +0.930*x*	
Cholesterol HDL mg/dl	*0.926*x*		
Triglycerides mg/dl	*-2.056+x*	*0.924*x*	
Creatinine urinaria[1] mg/dl	*0.896*x*	*-3.126+1.112*x*	
Glycosylated Hemoglobin %		*0.888*x*	
Reactive Protein C (PCR) mg/dl			*0.073+0.731*x*

Reactive Protein C (PCR) mg/dl
[1] *the adjusted values < 0 are replaced by 0.5*

Nutrients in the diet

Data on the diet of the participants were gathered with an abbreviated version of the questionnaire of frequency of foods (FFQ initials in English) developed and validated specifically to evaluate the ingestion of nutrients in the adult population in Costa Rica in the coronary illness study (Ek-Sohemy, Baylin et al 2001; Kabagambe, Baylin et al 2001; Kabagambe, Baylin et al 2005).

The original FFQ contains 147 foods, many of them of the specified in the Costa Rican diet, and it requires around 45 minutes of interview (Kabagambe, Baylin et al 2005). That study was based on detailed information on about 2000 residents in the Central Valley of Costa Rica, ages 60 and older who were the population controls for another equal amount of cases of myocardial heart attacks. The FFQ asks for the average consumption during the year prior to the survey, providing 9 possible answers to categorize the consumption frequency, which range from "never or less than once a month" to "6 or more times a day." The frequencies are converted in the computer to a daily number of times and it estimates the consumed quantity. The FFQ also asks for the consumption of vitamins and nutritional supplements, the brands of cooking shortening, oil margarine used, and certain kinds of food preparation.

That study estimated for each individual the energy ingestion and of several dozens of nutrients multiplying the frequency of consumption of each food by the nutritional content of the respective portion using values of composition of the foods from the database of the Department of Agriculture of the US, in addition to data from producers and published reports as well as specific data for Costa Rica regarding the nutritional content of foods and local food preparation practices.

Using stepwise regression --to optimize the goodness-of-fit and the parsimony of the model that explains the nutrient with the foods-- CRELES researchers reduced the original FFQ to a 10 minute interview by identifying the minimum number of foods that maximizes the variance explained in a selection of nutrients of interest to CRELES (Appendix 3). In this way 27 tracer foods were identified, which together with the brand of oil or shortening and the food preparation practice, explain 85% or more of the variances in seven nutrients and 75% or more in 17 nutrients (Table 4). The abbreviated FFQ of CRELES was defined with these purposes: (1) to have valid estimates at the individual level of the consumption of some nutrients of interest and (2) to minimize the interview time. For this the data of the control group of the "Study of Coronary Health of Costa Rica" was used (Kabagambe, Baylin et al 2005).

The ingestion of those 27 nutrients by the CRELES participants is estimated based on the abbreviated questionnaire of tracer foods in combination with the determined regression equations, and with the detailed data of the study of coronary health. A database of the nutritional content of the foods and complex computation programs allow for moving from the original FFQ to more than a hundred of nutrients.

The tracer foods defined in this way are sometimes counterintuitive or go against previous knowledge. For example, although rice is an important determinant of the consumption of calories in Costa Rica, this food is not a good tracer because its consumption is practically universal in the country. After consolidating all the tracer foods of the different nutrients, the result was the list of 27 foods of the abbreviated FFQ. The correlation coefficients among the 18 nutrients estimated in this way and the originals are on the average of 0.90, with range from a minimum of 0.84 for iron of 0.94 for cholesterol and 0.99 for alcohol.

Table 4: Goodness-of-fit (R2) of ingestion of selected nutrients with an abbreviated questionnaire of 27 tracer foods.

Nutrient	R^2
Total energy, kcal/d	0.81
Proteins, g/d	0.80
Carbohydrates, g/d	0.76
Glycemic Load, g/d	0.78
Total fats, g/d	0.85
Saturated fats, g/d	0.84
Monounsaturated fats, g/d	0.88
Polyunsaturated fats, g/d	0.82
Omega-6 fatty acid, g/d	0.81
Omega-3 fatty acid, g/d	0.85
Trans fats, g/d	0.85
Cholesterol, mg/d	0.94
Fiber, g/d	0.76
Alpha-Tocopherol, mg/d	0.78
Gamma-Tocopherol, mg/d	0.86
Calcium, mg/d	0.84
Alcohol, g/d	0.99

N = 2.200 (it is decreased slightly in some nutrients due to missing values)
Source: database of the Study of Coronary Health

Research Ethics

The study was approved by the Ethical Science Committee of the University of Costa Rica in the March 17, 2004 session (reference: VI-763-CEC-23 -04), research project number 828-A2 -825. Appendix 1 includes the most recent version in the informed consent approved by this Committee. All the databases of the study have been made anonymous (the name or identifier has been removed) to avoid risks to the privacy of the participants.

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