
Cardio-Metabolic Health Venezuelan Study (EVESCAM): Design and Implementation.

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Abstract. The EVESCAM (Estudio Venezolano de Salud Cardio-Metabólica) is the first national, population survey in Venezuela, designed to examine the prevalence of diabetes and cardio-metabolic risk factors and its relationship with lifestyle. It is a cross-sectional, cluster sampling study, which recruited 4454 participants aged ≥ 20 years. The data were collected in community health-care centers by trained health professionals and medical students. The data collected from each subject included, after informed consent, structured questionnaires

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(clinical, demographic, physical activity, nutritional and psychological), anthropometric measurements (weight, height and waist circumference), body fat by bioelectrical impedance, hand grip, blood pressure, electrocardiogram, and biochemical measurements (standard 75 g oral glucose tolerance test, total cholesterol, HDL-cholesterol, LDL-cholesterol and triglycerides). The data will be used to estimate the prevalence of overweight, obesity, prediabetes, diabetes, hypertension, dyslipidemias, sarcopenia and metabolic syndrome; and to examine their relationships with lifestyle factors. The risk of coronary heart disease and impaired glucose regulation will be estimated using the Framingham Coronary Heart Disease Risk Score and the Latin America adaptation of the Finnish Diabetes Risk Score (LA-FINDRISC), respectively. These results will guide national cardiovascular and diabetes prevention strategies, and will be available for government agencies to help in the implementation of public health policies.

Estudio Venezolano de Salud Cardio-Metabólica (EVESCAM): Diseño e Implementación.

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Palabras clave: diabetes mellitus; factores de riesgo; epidemiología; Venezuela.

Resumen. El EVESCAM (Estudio Venezolano de Salud Cardio-Metabólica) es el primer estudio poblacional de muestreo nacional en Venezuela diseñado para examinar la prevalencia de diabetes y factores de riesgo cardio-metabólico, y su relación con el estilo de vida. Se trata de un estudio transversal de muestreo por conglomerados, reclutando 4454 participantes de 20 años o más. Los datos fueron recogidos en centros de salud de la comunidad por profesionales de salud y estudiantes de medicina entrenados. Después del consentimiento informado, los datos recolectados en cada sujeto incluyeron: cuestionarios estructurados (clínico, demográfico, actividad física, nutricional y psicológico), medidas antropométricas (peso, talla y circunferencia de cintura), grasa corporal por impedancia bioeléctrica, fuerza de aprehensión de la mano, presión arterial, electrocardiograma y medidas bioquímicas (prueba de tolerancia a la glucosa oral estándar con 75 g de glucosa, colesterol total, colesterol HDL, colesterol LDL y triglicéridos). Los datos se utilizarán para estimar la prevalencia de sobrepeso, obesidad, prediabetes, diabetes, hipertensión arterial, dislipidemias, sarcopenia y síndrome metabólico; y para examinar sus relaciones con factores de estilo de vida. El riesgo de cardiopatía coronaria y de alteración de la regulación de la glucosa se calculará utilizando la puntuación de riesgo de la enfermedad coronaria de Framingham y la adaptación para Latinoamérica de la puntuación finlandesa del riesgo de diabetes (LA-FINDRISC), respectivamente. Estos resultados guiarán las estrategias nacionales de prevención cardiovascular y diabetes, y estarán disponibles para que las agencias gubernamentales ayuden en la implementación de las políticas de salud pública.

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INTRODUCTION

The increasing prevalence of obesity and unhealthy lifestyle habits are the major drivers for the epidemics of type 2 diabetes (T2D) and cardiovascular disease (CVD), especially in developing countries (1) where they impose a high burden on health care costs (2). Globally, the number of adults with diabetes increased from 108 million in 1980 to 422 million in 2014 (3) and, according to the International Diabetes Federation (IDF), this number is expected to rise to 642 million by 2040 (4). A similar increase is projected to occur in Latin America (LA) (from 9.4% in 2015 to 11.9% in 2040) (4). However, not always the data sources are optimal. The diabetes prevalence by age and sex reported in the diabetes atlas of the International Diabetes Federation (IDF), was obtained from 133 studies in 91 countries, of which only 37 (28%) were national studies (1). In fact, the diabetes prevalence reported for Venezuela was extrapolated from Brazil (1). The trend of coronary heart disease mortality between the years 1970 and 2000 increased in Venezuela (5), and the absolute number of deaths due to heart disease and T2D also rose between 2006 and 2009 (6).

After a comprehensive literature search of cardio-metabolic risk factors rates including 22 studies, regional disparities in the eight regions of Venezuela were documented (7). The weighted prevalence of diabetes (7.7%) and prediabetes (11.2%) in Venezuela has been also reported (8). Until now, the most representative study developed in Venezuela, is the Venezuelan Metabolic Syndrome, Obesity and Lifestyle Study (VEMSOLS), comparing the prevalence of cardio-metabolic and lifestyle risk factors in three regions of Venezuela. Preliminary results in a rural Andean municipality have been reported (9, 10). Unhealthy dietary habits and high rates of physical inactivity has been also described (7); however, no national population survey has

been developed in Venezuela (6).

Considering the high prevalence of cardiovascular risk factors and adverse trends in CVD (5) and T2D mortality (3), it is critical to assess the magnitude of the problem and its drivers to design successful preventive measures. Therefore, the objective of the EVESCAM is to determine the prevalence of cardio-metabolic risk factors, and lifestyle habits and their relationships in individuals of both genders over 20 years of age in a national sample of Venezuela. This paper describes the objectives, design, and implementation of this study.

MATERIALS AND METHODS

EVESCAM is a population based, observational, cross-sectional and cluster sampling study, designed to recruit and evaluate the cardio-metabolic health of selected subjects aged ≥ 20 years between 2015 and 2017.

Venezuelan Population and Regions

The Bolivarian Republic of Venezuela consists of 23 states, a Capital District and federal entities, distributed in 335 municipalities. The estimated population in 2011 was 27,150,095 inhabitants (11). Sixty-six percent of the population was between 15 and 64 years old (12). Venezuelan states are distributed into 8 regions: 1) Capital (DC Capital, Miranda and Vargas), 2) Central (Aragua, Carabobo and Cojedes), 3) Western (Falcón, Lara and Yaracuy), 4) North-Eastern (Anzoátegui, Delta Amacuro, Monagas, Nueva Esparta and Sucre), 5) Guayana (Amazonas and Bolívar), 6) Andeans (Mérida, Táchira and Trujillo), 7) Zulia (Zulia) and 8) Llanos (Apure, Guárico, Barinas and Portuguesa). Each region has particularities regarding geography, climate, natural resources, population density, urban/rural proportion, food availability, typical food and meal-based eating patterns, which can influence the public health

recommendations for the prevention and treatment of CVD and T2D.

Participant Sampling and Recruitment

The sampling design was set up to achieve two objectives. First, that there was a sample size enough to estimate accurately the prevalence, mean values and distribution of cardiometabolic risk factors and lifestyle habits, stratified by region, age and other demographic variables. Second, to assess the relationships among risk factors, lifestyle indicators and predictive risk scores for cardiovascular disease and T2D.

Initially, 23 cities from the eight regions—one to four cities per region—were chosen (Table I). Each selected city was stratified by municipalities. Two municipalities in each city, then two parishes in each municipality, and finally two locations in each parish, which is the conglomerate or cluster, were randomly selected. After selecting, map and census of each location were required to delimit the streets or blocks, and to select the households to visit. After selecting the sector to be surveyed at each location, the visits to households started from number 1 onwards skipping every two houses. That is, the household visited were 1, 4, 7, 10, 13, 16 and so on. If the number of people required after covering all households of this sequence was not achieved, the sampling continued on households 2, 5, 8, 11, and so on, until obtaining the number of subjects required to complete the sample from that sector.

In each household, all members aged ≥ 20 years were eligible to enter the study and were invited to participate. There was no age limit above 20 years. Exclusion criteria were current pregnancy, inability to stand or communicate, or refusal to participate in the study by not signing the informed consent. After reading the informed consent and agreeing to participate in the study, a signature was obtained. Then, identification data and a social status questionnaire

were collected from each subject. Finally, subjects were invited to assist to the physical and metabolic evaluation in a nearby health center and an instructive that includes a detailed explanation of the evaluation procedures was provided and explained.

The sample size was calculated to detect a diabetes prevalence (the lowest prevalent condition reported in Venezuela) of 7.7% (7) with a standard deviation of 1.55%, which allows to calculate a 95% confidence interval (95% CI). The minimal estimated number of subjects to be evaluated is 2940. Considering a minimal expected response rate of 70%, the final sample size was 4200, representing the proportions of the country in terms of age, sex, race, social status and proportion of rural and urban populations (Table I). In each region, at least 525 subjects were recruited. The sampling also considered that is necessary to evaluate at least 70% of recruited subjects in each region. Thus, if after recruiting 525 subjects the evaluation of at least 70% has not been achieved, the recruitment was to continue until that response rate was reached in each region. Finally, 4454 subjects (254 added for oversampling) were recruited (86.3% urban and 13.7% areas). Of these, 3445 (505 more than minimal required) were evaluated, for a response rate of 77.3%.

Assessments of lifestyle habits and socio-demographic variables

Questionnaires were interviewer-administered and collected participant's identification, location and contact information, family medical history, personal health and medical history including cardiovascular and T2D risk, social status, use of health care facilities, tobacco history, depression and/or anxiety, heart failure symptoms, alcohol consumption and current physical activity. Dietary intake was ascertained using both a food frequency questionnaire adapted to the Venezuelan population and a Mediterranean

TABLE I
CITIES, FIELD CENTERS, AND NUMBER OF PARTICIPANTS RECRUITED
IN THE EVESCAM FROM EIGHT REGIONS OF VENEZUELA

Region	Cities and towns	Projected to recruit	Recruited	Urbal/Rural	Field Centers
Western	Barquisimeto	391	434	Urban	Universidad Centro-Occidental "Lisandro Alvarado" (UCLA)
	San Felipe	39	56	Rural	
	Chichiriviche	95	80	Urban	
Central	Valencia	465	420	Urban	Universidad de Carabobo (UC)
	San Carlos	60	105	Rural	
Capital	Caracas	272	292	Urban	Universidad Central de Venezuela (UCV)
	Los Teques	33	46	Urban	
	Guatire	140	156	Urban	
	Guatire	80	89	Rural	
Andeans	Mérida	250	255	Urban	Universidad de Los Andes (ULA)
	Timotes	80	85	Rural	
	Tovar	40	46	Urban	
	La Mesa de Esnujaque	155	160	Urban	
Zulia	Maracaibo	525	450	Urban	Universidad del Zulia (LUZ)
	Maracaibo		75	Rural	
North-Eastern	Barcelona	75	78	Urban	Universidad de Oriente (UDO)
	Barcelona	75	75	Rural	
	Lecherías	120	126	Urban	
	Maturín	206	231	Urban	
	Margarita	49	56	Urban	
The Llanos	Calabozo	150	157	Urban	Universidad Nacional Experimental de los Llanos Centrales Rómulo Gallegos (UNERG)
	San Juan de los Morros	160	196	Urban	
	Valle de La Pascua	155	158	Urban	
	Valle de La Pascua	60	64	Rural	

TABLE I. (*Continue*)

Region	Cities and towns	Projected to recruit	Recruited	Urbal/Rural	Field Centers
Guayana	San Félix	150	151	Urban	Universidad de Oriente (UDO)
	Ciudad Bolívar	330	354	Urban	
	Maniapure	45	59	Rural	
Total	Venezuela	4200	4454	Urban 86.3% Rural 13.7%	

diet adherence questionnaire (Table II).

Non-invasive measurements

Blood pressure was measured twice, with five minutes intervals, in the right arm, supported at heart level, in a sitting position, after five minutes of rest, with a validated (18) oscillometric sphygmomanometer (Omron HEM-705C Pint® Omron Healthcare CO., Kyoto/Japan). Height was measured using a portable stadiometer (Seca 206® seca gmbh & co. Hamburg /Germany). Weight and body fat (bioimpedance) were measured with the lightest possible clothes, without shoes, using a calibrated scale (Tanita UM-081 ® Japan). Body mass index was calculated (BMI: weight[kg]/height[m]²). Two measures of waist circumference were obtained with a non-stretchable metric tape, at the iliac crest, in a horizontal plane with the floor at the end of expiration, the average between both measures will be used. Handgrip strength was measured with a dynamometer (Jamar J00105® Lafayette Instrument Co., UK), in sitting position, recording the maximum isometric strength of both the right and the left hand. A portable, handheld, 1-lead/channel electrocardiograph (Omron HCG-801® Omron Healthcare CO., Kyoto/Japan) was used.

Invasive measurements

Blood specimens were collected at each site according to a standardized protocol. A blood sample was collected soon after arrival to the

health center, with at least 8-hours of fasting period, and a second collection was done following a 2-hour oral glucose tolerance test (Table III). Frozen specimens were shipped to the central laboratory for analysis. After the post-load venipuncture, participants were provided with a snack. Serum aliquots were stored at -40° C, placed in dry ice and transported to the Cardiometabolic Unit 7 in Barquisimeto, and stored at -40 °C until analyses were performed. A repository of serum was established at the central laboratory for future analysis.

Definition of qualitative and quantitative variables

Variables evaluated and its definitions are presented in table IV.

Data analysis

Study forms will be reviewed to ensure that they have complete data before data entry. All calculations will be performed using SPSS 20 software (IBM Corp. Released 2011. IBM SPSS Statistics Windows, Versior. 20.0. Armonk, N.Y: IBM Corp). All continuous variables will be initially tested for normality (Kolmogorov-Smirnov and Q-Q plots). The measures of central tendency and dispersion that will be used to describe the results and the next step in selecting statistical analysis will depend on the type of variable and distribution, and the number of groups to be compared. Normally distributed continuous variables will be presented as

TABLE II
EVESCAM QUESTIONNAIRES

Questionnaires	Description
Questionnaire 1: identification and clinical data	
Identification data*	Recruiter code, visit date, interviewer code, recollection date, coordinator code, city, and field center code. Recruited subject data: first name, last name, identity number, birth date, age, gender, phone number, race, most frequent health care center visited, academic level
Family medical history	Based on determining the presence of family risk factor
Personal medical history	Based on determining the presence of diseases, risk factors, and treatments
Psychobiologic habits	Based on current and former tobacco use and alcohol consumption habits
Questionnaire 2: physical activity	
International Physical Activity Questionnaire (IPAQ) short version (13)	To assess physical activity determining the frequency and time dedicated in the last 7 days to activity: vigorous, moderate, walking and time sitting
Questionnaire 3: anxiety and depression symptoms	
Hospital Anxiety and Depression Scale (HADS) (14)	To interrogate symptoms of anxiety and depression
Questionnaire 4*: social strata	
Graffar method modified by Méndez-Castellano (15)	To determine social status, four variables were considered: 1. source of income; 2. profession of householder; 3. educational level of the mother; 4. housing conditions
Questionnaire 5: heart failure symptoms	
The New York Heart Association (NYHA) functional class (16)	To place those who report suffering from heart failure, in one of four categories based on the limitation during physical activity
Questionnaire 6: frequency of food consumption	
Food frequency questionnaire	To quantify the number of portions of each food or food group consumed daily, weekly or monthly
Questionnaire 7: Mediterranean diet adherence	
Mediterranean diet adherence questionnaire (17)	To evaluate the adherence to Mediterranean diet
Informed consent	To document that each individual agrees to participate in the study. After being read and explained to the subject, the informed consent needs to be signed

* Questionnaires applied in recruited subjects at home invitation

TABLE III
LABORATORY TESTS

Tests	Description
Venipuncture	To obtain 10 mL of fasting blood sample and then centrifugation
Oral glucose tolerance test	2 hour post-load 75 g of anhydrous glucose was obtained
Additional samples	5% of the sample will be randomly selected for external validation
Blood tests	Fasting blood glucose, total cholesterol, triglycerides, LDL-cholesterol and HDL-cholesterol

Abbreviations: HDL: high density lipoprotein. LDL: low density lipoprotein

mean \pm standard error of the mean (SEM) and differences will be assessed by Student t-test or analysis of variance (ANOVA). Not normally distributed variables will be presented as median \pm interquartile range (IR) and the differences will be assessed by the Mann-Whitney U test or Kruskal-Wallis test. Proportion of subjects with obesity, dyslipidemia, hypertension, prediabetes, diabetes, metabolic syndrome, cardiovascular risk, and poor eating habits defined as a lower adherence (lower quintiles) to Mediterranean diet, will be presented as prevalence rates and 95% confidence intervals. For analysis of prevalence data, the population will be divided into six age groups (20-29, 30-39, 40-49, 50-59, 60-69, 70+). To compare the prevalence rates of each variable among groups, Chi-square test will be used. To define the associated risk to each factor in the development of CVD and T2D, a multiple regression model will be performed. The level of statistical significance will be a p-value < 0.05.

Protocol standardization

To standardize the examination and measurement process across health centers, each of the eight regions is coordinated by a team centralized in a university (field centers). A total of seven universities participated in the study (Table I). A central laboratory and a central data reading center serve as foci for protocol develop-

ment, training and certification of staff, centralized measurements or readings, and data quality assessment and control. The Central Laboratory at the Cardiometabolic Unit and Universidad Centro-Occidental "Lisandro Alvarado" in Barquisimeto, Lara State, Venezuela, standardizes the blood processing and shipping procedures, conducts all laboratory assays, implements blind replicate measurements for 5% of samples, provides technical support to the regions and transfers the study results to the coordinating center. The electrocardiogram and the nutrition data will be analyzed at the same center. Details on the recruitment, evaluation, protocol standardization and methodology including laboratory collection, processing and analysis can be found in online manuals (<http://www.svmi.web.ve/>).

Training and guarantee of quality

To be able to fully capacitate the personnel, special sessions in filling the questionnaires were implemented. Also, a rigorous preparation was applied to the trainees so that the anthropometric measures could be done precisely; this included height, weight and abdominal circumference. For the physical examination, special sessions on taking of blood pressure supervised by a qualified instructor were done. Personnel were trained in using portable bioimpedance meter, dynamometer and electrocardiograph.

TABLE IV
VARIABLE DEFINITIONS

Variable	Definition
BMI categories (19)	<ul style="list-style-type: none"> - Underweight < 18.5 kg/m² - Normal weight 18.5 - <25 kg/m² - Overweight 25 to <30 kg/m² - Obesity ≥ 30 kg/m² Abdominal obesity according to proposed Latin American standards for waist circumference (19): <ul style="list-style-type: none"> - ≥ 94 cm in men - ≥ 90 cm in women Levels of total body fat percent for obesity according by WHO (20): <ul style="list-style-type: none"> - >25% in men - >35% in women
Hypertension	<ul style="list-style-type: none"> -Systolic blood pressure ≥ 140 mmHg or -Diastolic blood pressure ≥ 90 mmHg or current antihypertensive treatment (21)
Dyslipidemia	According to the NCEP/ATPIII (22): <ul style="list-style-type: none"> -Hypercholesterolemia: ≥ 240 mg/dL of total cholesterol -Elevated LDL-c ≥ 160 mg/dL -Atherogenic dyslipidemia: triglycerides ≥150 mg/dL + low HDL-c <40 mg/dL in men and < 50 mg/dL in women -Mixed dyslipidemia: triglycerides ≥ 150 mg/dL + total cholesterol ≥ 240 mg/dL
Prediabetes and diabetes	According to the American Diabetes Association (23). <ul style="list-style-type: none"> -Diabetes: fasting plasma glucose was ≥ 126 mg/dL or 2-hours post oral glucose tolerance test (75g) ≥ 200 mg/dL or A1c ≥ 6.5% or if antidiabetic medications were used. -Prediabetes: fasting plasma glucose ≥ 100 mg/dL and <126 mg/dL or glucose level after a 75g oral glucose tolerance test ≥ 140 mg/dL and < 199 mg/dL or A1c ≥ 5.7% and <6.4%.
Metabolic syndrome	According to the harmonized definition 2009 Joint Interim Statement (24), as presence of at least of 3 of the following: <ul style="list-style-type: none"> -Abdominal obesity (waist ≥ 94 cm in men, ≥90 cm in women) -Elevated triglycerides ≥150 mg/dL -Low HDL-c <40 mg/dL in men, < 50 mg/dL in women -Raised blood pressure ≥ 130/85 mmHg or antihypertensive treatment -Fasting blood glucose ≥ 100 mg/dL or self-reported diabetes
Coronary heart disease risk score	According to the Framingham Risk Score (25)
Type 2 diabetes risk	According to modified Latin American Finnish Diabetes Risk Score (LA-FIN-DRISC), including waist circumference cut-off values adapted to the region (26, 27)

Abbreviations: ATPIII: Adult Treatment Panel III. HDL: high density lipoprotein. LDL: low density lipoprotein. NCEP: National Cholesterol Education Program. WHO: World Health Organization.

Training in blood samples extraction, preservation and proper transportation were taking into account carefully.

Study centers and governance

A Steering Committee (consisting of the principal investigators of both the coordinating institution and coordinating center, principal investigators of each region and universities, members of the Internal Medicine Venezuelan Society [SVMI] and international consultants provides the scientific and procedural direction for the EVESCAM. There are other committees under the oversight of the Steering Committee: ancillary studies, publications, operation/examination, sampling/recruitment and data management, quality control and questionnaires. The EVESCAM budget is administrated at the Office of Management and Budget of the SVMI by an ad hoc foundation named Foundation for Public Health and Epidemiology Research in Venezuela (FISPEVen). This foundation also coordinates the ancillary studies.

Ethical considerations

The study protocol was designed in compliance with the Helsinki declaration and it was approved by the National Bioethics Committee (CENABI). Consent from all participants were obtained and filed.

DISCUSSION

EVESCAM is the first study obtaining information of cardio-metabolic risk and lifestyle factors in a sample representative of the entire population of Venezuela. The EVESCAM is designed to inform health care providers and the public health community, on the frequency of cardio-metabolic risk factors and diseases such as overweight, obesity, prediabetes, diabetes, hypertension, dyslipidemias, sarcopenia, metabolic syndrome and its relationships with lifes-

style factors and the risk of coronary heart disease risk and impaired glucose regulation. Smoking, physical activity and nutritional habits also will be obtained.

Two well designed cross-sectional studies have reported the prevalence of several cardio-metabolic risk factors in specific regions of Venezuela. The first, study of risk factors for coronary heart disease in Zulia state, in 3108 subjects, for over 20 years, in the Zulia region. This study reported that the age-adjusted prevalence of metabolic syndrome and atherogenic dyslipidemia were 31.2% and 24.1%, respectively (28). The second study, the CARMELA, was designed to assess the prevalence of CVD risk factors, carotid plaques, and carotid intima-media thickness in 11150 individuals, aged 25 to 64 years, living in seven major Latin America cities. The sample from Barquisimeto, Venezuela, compared with the other cities, had a higher prevalence of metabolic syndrome (25.8%, ranked 2nd), hypertension (24.7%, ranked 2nd) and obesity (25.1%, ranked 3rd); but a lower prevalence of diabetes (6.0%, ranked 5th), hypercholesterolemia (5.7%, ranked 7th), and smoking (21.8%, ranked 7th) (29).

A review of the prevalence studies published in Venezuela revealed that the weighted prevalence of diabetes was 7.7% (8). However, the two studies mentioned above included 73% of the 6807 participants. The rest (n=1851 subjects) are from smaller studies representative of local parishes or municipalities. More recently, in a cross-sectional study in 2230 individuals (52.6 % females) from Maracaibo (Zulia State), a total 8.4 % were found to have DM2, and 19.5 % had impaired fasting glucose (30). Therefore, a national survey is a necessity.

Considering that the EVESCAM include a nationally representative sample, it will provide large-scale information regarding the associations of life-style factors with the burden of some non-communicable chronic diseases. This

information will allow the promoting of public health policies in Venezuela. Any research component missing from the core study, could be later the subject of ancillary studies whose procedures and policies are published in the SVMI web site (<http://www.svmi.web.ve/>).

EVESCAM alignment with policies of research in Venezuela

The objectives of the EVESCAM study are consistent with the stated in the Article 13 of the Organic Law of Science, Technology and Innovation (LOCTI) in Venezuela (31). EVESCAM is a project that reaches the public sector at different levels (municipalities, states and at national level), and establishes further agreement between the private sector and the scientific community. Furthermore, according to Article 14 of LOCTI, the project EVESCAM is oriented within the lines of action established by the national government, which include: a. Paragraph 1: Research and development to improve the quality of life, b. Paragraph 2: Generation of knowledge and promotion of human talent and c. Paragraph 4: Strengthening and coordination of scientific cooperation networks and technological innovation (31). The information generated from the EVESCAM undoubtedly will be the guide for cardiovascular and diabetes prevention strategies and will be available for government agencies to help in the implementation of public health policies.

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Appendix

EVESCAM Institutions and Staff

Coordinating Institution .Venezuelan Society of Internal Medicine (SVMI). Caracas, Venezuela.

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