CLINICAL RESEARCH STUDY

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CARMELA: Assessment of Cardiovascular Risk in Seven Latin American Cities

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ABSTRACT

OBJECTIVE: This cross-sectional, population-based observational study using stratified multistage sampling assessed the prevalence of cardiovascular risk factors and carotid plaques and measured carotid intima-media thickness in individuals living in major cities in 7 Latin American countries.

PATIENTS AND METHODS: The study comprised individuals (n = 11,550) aged 25 to 64 years, living in Barquisimeto, Bogota, Buenos Aires, Lima, Mexico City, Quito, and Santiago. Data on anthropometric parameters, blood pressure, fasting glucose, total and high-density lipoprotein cholesterol, triglycerides, carotid intima-media thickness, carotid plaque, and smoking status were collected through household interviews and clinical, biochemical, and sonographic measurements.

RESULTS: The overall prevalence rates (ranges across cities) were as follows: hypertension (≥140/90 mm Hg or pharmacologic treatment), 18% (9%-29%); hypercholesterolemia (total cholesterol ≥240 mg/dL), 14% (6%-20%); diabetes (glycemia ≥126 mg/dL or self-reported diabetes), 7% (4%-9%); metabolic syndrome, 20% (14%-27%); obesity (body mass index ≥30 kg/m^2), 23% (18%-27%); smoking, 30% (22%-45%); and plaque, 8% (5%-14%). The mean intima-media thickness was 0.65 mm (0.60-0.74 mm).

CONCLUSION: The prevalence of hypertension mirrored the world average in 3 cities but was lower in the rest. Hypercholesterolemia was highly prevalent even in countries of different socioeconomic levels. The prevalence of diabetes was similar to that in the developed countries. Tobacco use in women living in Santiago and Buenos Aires was among the world's highest. Intima-media thickness and carotid plaque prevalences varied widely.

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Latin America is undergoing an epidemiologic transition,[1,2] acquiring urban-industrial lifestyles typically associated with an increasing prevalence of cardiovascular disease and diabetes. Hypertension, hypercholesterolemia, tobacco use, or their combination contributes to three quarters of the cases of cardiovascular disease.[3] Educational and public health measures based on the knowledge of population risk factors can decrease this disease burden. Previous limited epidemiologic assessments conducted in Latin America have been hampered by inconsistencies in risk factor definitions, sampling, and assessment methods.[4,5] Disparities in health resources in Latin America call for country-specific epidemiologic data to generate rational policies for surveillance, prevention, and intervention.

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The objectives of the Cardiovascular Risk Factor Multiple Evaluation in Latin America (CARMELA) study were to assess the prevalence of cardiovascular risk factors and common carotid far wall intima-media thickness distributions in individuals living in 7 Latin American cities (Barquisimeto, Venezuela; Bogota, Colombia; Buenos Aires, Argentina; Lima, Peru; Mexico City, Mexico; Quito, Ecuador; and Santiago, Chile), all of which are capitals of their respective countries, except Barquisimeto.

CLINICAL SIGNIFICANCE

- The prevalence of cardiovascular risk factors and the distribution of common carotid artery intima-media thickness were heterogeneous among the persons in 7 Latin American cities; age and sex trends were consistent with elsewhere in the world.
- Hypertension and hypercholesterolemia prevalence generally approximated world averages.
- Diabetes prevalence was in the range of the developed world.
- Rates of smoking among women in Santiago and Buenos Aires are among the world's highest.

PATIENTS AND METHODS

This study was conducted in accordance with the Declaration of Helsinki, Guidelines for Good Clinical Practice, and local bioethics regulations and laws. All subjects provided written informed consent.

Sampling and Survey

CARMELA was designed to enroll approximately 1600 participants per city, with equal numbers of men and women in each of four 10-year age groups. This number was selected on the basis of the sample sizes in similar studies, expected variation in risk factors, and limitations dictated by study resources. Cities were first divided into geographic sectors and then into primary sampling units (city blocks or other appropriate areas), which were randomly selected for further sampling. Households present in selected primary sampling units were placed into 4 categories, and then a systematic sample was obtained within each category. In category 1, all eligible and consenting residents aged 25 to 64 years were interviewed; in category 2, only residents aged 35 to 64 years were interviewed; in category 3, only residents aged 45 to 64 years were interviewed; and in category 4, only residents aged 55 to 64 years were interviewed. The sampling fraction in each category was determined so that an equal probability sampling was obtained within each sex–age group. This strategy was conceived to minimize the number of households to be visited, taking into account that group sizes decrease with age. Sampling was also adjusted on the basis of nonresponse rates from a pilot study of 50 enrollees per city. Each city resident between the ages of 25 and 64 years (and ultimately everyone in each defined age group) had a predetermined non-zero probability of selection. Anyone within the age limits residing at selected addresses was eligible for inclusion; subjects were included only if they completed the survey and clinical visit. Exclusion criteria comprised persons residing at addresses that were not households or were in marginal areas considered to endanger interviewers and persons visiting at the selected addresses.

Interviewers, trained and certified by CARMELA investigators, administered a questionnaire customized from well-known cardiovascular epidemiologic questionnaires (WHO STEPwise approach to surveillance and the US Behavioral Risk Factor Surveillance System) to collect information on demographics, hypertension, hypercholesterolemia, diabetes, and smoking. Participants visited a designated health care institution for anthropometric and clinical measurements, were reimbursed for their transportation and breakfast, and were provided their clinical, laboratory, and intima-media thickness results.

Clinical Measurements

Standardization of Assessments. Methods and devices for obtaining anthropometric and clinical measurements were standardized across all centers, and measurements were obtained by health personnel trained, certified, and supervised by CARMELA investigators. Standardization across laboratories and quality control followed the procedures of the Buenos Aires external quality assessment program, with fortnightly monitoring of performance.[6] Board-certified vascular sonography physicians underwent centralized training and certification by CARMELA investigators, and submitted ultrasound images of 3 random subjects and a standard phantom to the central laboratory (Intelligence in Medical Technologies, Paris, France) for quality certification before being allowed to collect study data.

Anthropometry. Subjects' height was measured without footwear. Weight and waist circumference were measured with subjects wearing only undergarments. Waist circumference was measured at the midpoint between the last rib and the iliac crest.

Blood Pressure. Two resting blood pressure readings were taken 5 minutes apart with a mercury sphygmomanometer with the subject seated; if different by more than 5 mm Hg, measurements were repeated until 2 concordant readings were obtained. Blood sampling was performed after blood pressure measurement.

Blood Lipids and Glucose. Subjects were to avoid using glycerin-containing laxatives for 48 hours and consuming glycerol-containing products for 24 hours before blood draws. For 12 hours before sampling, subjects could consume only water, black coffee, or unsweetened tea; fast-

ing state was confirmed. Subjects were instructed to take their usual medications except antidiabetic medications, which were not to be taken until after blood was drawn. Glycemia was assayed within 6 hours. Serum was assayed for total cholesterol, high-density lipoprotein cholesterol, and triglycerides; low-density lipoprotein cholesterol was calculated.

Clinical Definitions. Hypertension was defined as systolic blood pressure ≥140 mm Hg and diastolic blood pressure ≥90 mm Hg, or current antihypertensive drug treatment.[7] Hypercholesterolemia was defined as total serum cholesterol ≥240 mg/dL,[8] and diabetes was defined as a fasting blood glucose level ≥126 mg/dL[9] or self-reported diabetes. Metabolic syndrome was defined as the presence of 3 or more of the following: waist >102 cm in men, >88 cm in women; triglycerides ≥150 mg/dL; high-density lipoprotein-cholesterol <40 mg/dL in men, <50 mg/dL in women; blood pressure ≥130/85 mm Hg; and fasting glucose ≥110 mg/dL or self-reported diabetes.[8] Obesity was defined as body mass index ≥30 kg/m^2. Smoking was defined as daily or occasional consumption of cigarettes, cigars, or pipe tobacco.

Ultrasonography. Far wall common carotid artery intima-media thickness and presence of plaque were evaluated according to the Mannheim consensus.[10] Common carotid arteries were examined by B-mode ultrasonography, using phased-array 7.5-MHz transducers. M'AthStd software (Intelligence in Medical Technologies, Paris, France) automatically measured intima-media thickness; measurements were taken over a 10-mm length and averaged, and the quality of acquisition was evaluated. Data were analyzed centrally (Intelligence in Medical Technologies, Paris, France). Plaque, defined as a protrusion into the lumen adding ≥50% to the thickness of the surrounding intima-media or a maximal thickness >1.5 mm, in the carotid bifurcation or along the carotid arterial tree was scored.

Statistical Analysis

Statistical processing addressed the non-equal probability character of the sample and structure of the design to generate data adjusted for the age and sex distribution of the population of each city. Two-sided 95% confidence intervals were estimated by PROC SURVEYMEANS (SAS Software, Release 9.1, Cary, NC), taking into account the multistage stratified sampling design via CLUSTER and STRATA statements. Cardiovascular risk was evaluated using the Framingham score algorithm,[8] which estimates the 10-year risk of cardiovascular events from systolic blood pressure, smoking status, total and high-density lipoprotein cholesterol, age, and sex.

RESULTS

Demographics

Table 1 shows the basic demographics of the 11,550 CARMELA participants. As expected per the study design, the mean age of participants was at the mid-range of study enrollment. Approximately 13% reported family members with cardiovascular disease, and 2% reported prior myocardial infarction or stroke.

Risk Factor Prevalence

The estimated prevalences of risk factors are presented in Table 2. Hypertension prevalences clustered into 2 groups: Barquisimeto, Buenos Aires, and Santiago had the highest prevalence (25%, 29%, and 24%, respectively), whereas Lima, Mexico City, Bogota, and Quito had a markedly lower prevalence (13%, 12%, 13%, and 9%, respectively). The prevalence of hypercholesterolemia was highest in Quito (20%) and lowest in Barquisimeto (6%), which was remarkably lower than in all other CARMELA cities.

Mexico City had the highest prevalence of diabetes (9%), metabolic syndrome (27%), and obesity (31%). In most cities, diabetes was more common among women; in Quito, it was nearly twice as prevalent in women (7%) as in men (5%). The exception was Buenos Aires, where diabetes was more prevalent in men (8%) than in women (5%). The sex distribution of metabolic syndrome and diabetes paralleled that of obesity in all cities.

Smoking was most prevalent in Santiago (45%) and Buenos Aires (39%), where rates were similar among men and women. In all other cities, fewer women than men smoked, with Quito having the smallest female to male ratio (11% vs 49%).

Carotid Ultrasonography

Ultrasonography was performed on 10,826 of 11,550 subjects (94%). Of these, 242 had a poor sonogram quality index for the right common carotid artery, and 205 had a poor sonogram quality index for the left common carotid artery. Intima-media thickness increased with age in both sexes in all cities (Table 3). Plaque ranged from 5% in Mexico City to 14% in Barquisimeto. The prevalence of plaque did not parallel intima-media thickness values. For example, Buenos Aires had the highest intima-media thickness but the second lowest prevalence of plaque; Barquisimeto showed the highest prevalence of plaque and the lowest mean intima-media thickness.

Risk Factor Combinations and Framingham Scores

The presence of multiple risk factors may synergistically increase an individual's overall cardiovascular risk. Therefore, prevalences of key risk factor combinations were assessed (Table 4). The distribution of overall cardiovascular risk in each city was assessed by Framingham risk scores[8] (Table 5); 11% to 18% of the population of each city showed an intermediate to high level of risk.

Table 1 Participant Demographics from the 7 Cities

	Barquisimeto	Bogota	Buenos Aires	Lima	Mexico City	Quito	Santiago
n	1848	1553	1482	1652	1722	1638	1655
Men (n, %)	713 (38.6%)	738 (47.6%)	734 (49.5%)	769 (46.6%)	833 (48.4%)	813 (49.6%)	783 (47.3%)
Mean age ± SD (y)	45.1 ± 11.3	45.1 ± 11.3	44.6 ± 11.7	43.6 ± 11.6	44.5 ± 11.3	44.4 ± 11.2	44.8 ± 11.2
Family history of premature CHD* (%, 95% CI)	14.8 (13.1-16.6)	10.8 (8.8-12.7)	18.1 (15.7-20.6)	10.0 (8.0-11.9)	9.3 (7.3-11.3)	9.2 (7.3-11.1)	15.5 (13.5-17.5)
Prior stroke or MI† (%, 95% CI)	1.2 (0.7-1.6)	1.1 (0.6-1.5)	2.5 (1.8-3.2)	2.2 (1.5-2.9)	0.7 (0.3-1.0)	2.8 (1.8-3.7)	2.4 (1.7-3.2)

SD = standard deviation; CHD = coronary heart disease; CI = confidence interval; MI = myocardial infarction.
*Family history of premature CHD, father or brother had fatal or nonfatal MI before age 55 years, or mother or sister had fatal or nonfatal MI before age 65 years.
†Prior stroke or MI, self-reported.

DISCUSSION

Cardiovascular risk was distributed heterogeneously across Latin America, with different risk factors concentrated in different cities. Hypertension prevalences were in 2 clusters: Buenos Aires, Barquisimeto, and Santiago had prevalences approximately 25%, comparable to worldwide (26%) and US (29%) prevalences,[11,12] whereas the other 4 cities had lower prevalences. The prevalence of hypercholesterolemia in Quito, Buenos Aires, Mexico City, and Santiago (15%-20%) was similar to that among US adults (17%).[13] Mexico City had the highest prevalence of obesity, metabolic syndrome, and diabetes. Male and female smoking rates were also dissimilar between cities. Consistent with most countries worldwide,[14] obesity was more prevalent in women than in men in all cities except Buenos Aires and Mexico City. Mexico City's prevalence of obesity was the highest, approaching that of Canada and the United States; those cities with the lowest prevalence were within a range common in transitional eastern Europe.[14]

CARMELA is among the first studies to compare the prevalence of metabolic syndrome among Latin American cities. Metabolic syndrome prevalence, assessed using the Adult Treatment Panel III definition, ranged from 14% in Quito to 27% in Mexico City. This is comparable to the National Health and Nutrition Examination Survey data on US adults (24%).[15] However, the CARMELA prevalences may be an underestimate; a recent consensus suggested that South and Central American men may manifest visceral adiposity at waist circumferences of ≥90 cm (substantially lower than the Adult Treatment Panel III cutpoint of >102 cm).[16]

Latin America is experiencing a diabetes pandemic, with Brazil and Mexico among the top 10 countries worldwide with the most cases of diabetes.[17] Even the lowest prevalence (5% in Lima) approximates that of the developed countries;[17] the highest prevalences (Mexico City and Bogota >8%) warn of an epidemic already under way.

The global obesity epidemic, fueled by urbanization, physical inactivity, and transition to high-fat diets, feeds into other cardiovascular risk factors. Obesity is an independent cardiovascular risk factor that contributes to elevated blood pressure and blood cholesterol, impaired glucose regulation, metabolic syndrome, and diabetes.[18,19] The "diseases of affluence" paradigm, which still informs much epidemiologic research, predicts that nutritional risk factors, such as obesity, increase in proportion to economic development and that higher income populations will be the earliest to adopt behaviors that increase risk.[20] However, as high-fat foods become inexpensive, body mass index and cholesterol levels in many populations increase at lower thresholds of income than previously assumed; nutritional risk factors emerge at earlier stages of economic development as diets change worldwide.[21] Thus, Ecuador is poorer and less developed than Argentina and Mexico;[22] however, Quito had the highest prevalence of hypercholesterolemia among CARMELA cities. Furthermore, in most

Table 2 Prevalence (as Percent and 95% Confidence Interval) of Major Risk Factors by City for the Overall Population and for Men and Women

	Barquisimeto	Bogota	Buenos Aires	Lima	Mexico City	Quito	Santiago
Hypertension*	24.7 (22.7-26.8)	13.4 (11.5-15.2)	29.0 (26.9-31.1)	12.6 (11.1-14.0)	11.7 (10.3-13.1)	8.6 (7.3-10.0)	23.8 (21.6-26.1)
Men	27.5 (23.7-31.3)	14.6 (11.9-17.2)	37.7 (34.3-41.1)	14.4 (12.2-16.7)	11.2 (8.9-13.6)	7.2 (5.6-8.7)	27.3 (24.1-30.5)
Women	22.9 (20.6-25.2)	12.4 (10.2-14.7)	21.7 (19.0-24.4)	10.7 (8.8-12.6)	12.1 (9.9-14.2)	10.1 (7.8-12.4)	20.7 (17.8-23.5)
Hypercholesterolemia†	5.7 (4.7-6.7)	12.0 (10.5-13.5)	18.7 (16.7-20.7)	11.6 (10.1-13.1)	16.4 (14.2-18.7)	20.2 (18.0-22.3)	15.3 (13.4-17.2)
Men	4.5 (3.0-6.1)	12.4 (9.9-14.9)	19.6 (16.8-22.4)	10.1 (8.2-12.1)	17.5 (14.4-20.7)	21.6 (18.2-25.0)	15.9 (13.3-18.5)
Women	6.5 (5.0-7.9)	11.7 (9.5-13.8)	17.8 (15.1-20.5)	13.0 (10.8-15.2)	15.4 (12.3-18.5)	18.8 (16.0-21.6)	14.8 (12.2-17.4)
Current smoking‡	21.8 (19.3-24.2)	22.2 (19.1-25.2)	38.6 (36.0-41.2)	26.6 (23.9-29.4)	27.3 (25.0-29.5)	29.9 (27.0-32.7)	45.4 (42.8-47.9)
Men	32.2 (27.7-36.7)	31.3 (27.1-35.5)	39.7 (36.2-43.2)	38.0 (34.2-41.7)	34.4 (30.2-38.5)	49.4 (45.9-52.9)	47.7 (44.2-51.1)
Women	14.9 (12.7-17.1)	15.0 (11.1-18.9)	37.7 (34.2-41.3)	15.4 (12.6-18.2)	21.0 (18.8-23.2)	10.5 (7.8-13.2)	43.3 (39.7-46.9)
Diabetes§	6.0 (5.0-7.0)	8.1 (6.8-9.5)	6.2 (4.8-7.7)	4.4 (3.4-5.4)	8.9 (7.7-10.2)	5.9 (4.8-7.1)	7.2 (5.9-8.6)
Men	5.6 (4.0-7.2)	7.4 (5.7-9.2)	7.9 (5.7-10.0)	4.3 (2.8-5.7)	8.0 (6.3-9.7)	4.6 (3.2-6.0)	6.8 (5.2-8.5)
Women	6.3 (5.0-7.5)	8.7 (6.8-10.6)	4.8 (3.3-6.4)	4.6 (3.2-5.9)	9.7 (7.8-11.6)	7.3 (5.6-8.9)	7.6 (5.6-9.6)
Obesity¶	25.1 (22.1-28.1)	18.0 (15.7-20.2)	19.7 (17.4-21.9)	22.3 (19.9-24.6)	31.0 (28.4-33.5)	16.3 (14.3-18.3)	26.6 (24.4-28.8)
Men	23.5 (18.8-28.3)	12.8 (10.1-15.5)	23.1 (19.8-26.3)	21.1 (18.0-24.3)	31.7 (28.0-35.4)	10.3 (8.2-12.5)	23.6 (20.4-26.8)
Women	26.1 (22.6-29.6)	22.0 (19.0-25.0)	16.8 (13.8-19.8)	23.4 (20.5-26.4)	30.4 (27.1-33.7)	22.4 (18.7-26.0)	29.4 (26.0-32.9)
Metabolic syndrome**	25.8 (23.3-28.4)	20.4 (18.2-22.5)	16.7 (14.8-18.6)	17.9 (15.9-20.0)	27.2 (24.9-29.4)	13.7 (11.9-15.6)	21.0 (18.9-23.1)
Men	26.3 (22.3-30.2)	18.7 (15.8-21.6)	21.7 (19.0-24.4)	15.8 (13.0-18.6)	26.3 (22.9-29.6)	7.5 (5.6-9.3)	19.0 (16.3-21.6)
Women	25.6 (22.9-28.3)	21.7 (19.0-24.4)	12.3 (9.6-15.1)	20.0 (17.3-22.8)	28.0 (24.4-31.6)	20.1 (16.9-23.4)	23.0 (20.0-26.0)

*Hypertension, blood pressure ≥140/90 mm Hg, or use of antihypertensive drugs.

†Hypercholesterolemia, total serum cholesterol >240 mg/dL.

‡Smoking, daily or occasional consumption of cigarettes, cigars, or pipe tobacco.

§Diabetes, fasting blood glucose level ≥126 mg/dL, or self-reported diabetes.

¶Obesity, body mass index ≥30 kg/m^2.

**Metabolic syndrome, presence of ≥3 of the following: abdominal obesity (waist >102 cm in men, >88 cm in women); triglycerides ≥150 mg/dL; high-density lipoprotein cholesterol <40 mg/dL in men, <50 mg/dL in women; blood pressure ≥130/85 mm Hg; fasting glycemia ≥110 mg/dL or self-reported diabetes.

Table 3 Mean Common Carotid Artery Far Wall Intima-Media Thickness and Prevalence of Carotid Plaque

Intima-media Thickness (mm)	Barquisimeto	Bogota	Buenos Aires	Lima	Mexico City	Quito	Santiago
Overall Mean (CI)	0.60 (0.59-0.60)	0.61 (0.61-0.62)	0.74 (0.74-0.75)	0.63 (0.63-0.64)	0.69 (0.69-0.70)	0.70 (0.69-0.71)	0.60 (0.59-0.60)
Men, mean (CI) for age groups:							
25-34 y	0.56 (0.55-0.57)	0.57 (0.56-0.58)	0.70 (0.68-0.71)	0.58 (0.57-0.59)	0.68 (0.67-0.69)	0.65 (0.64-0.66)	0.55 (0.54-0.55)
35-44 y	0.60 (0.59-0.61)	0.60 (0.59-0.61)	0.74 (0.73-0.75)	0.63 (0.62-0.65)	0.69 (0.68-0.69)	0.69 (0.68-0.70)	0.61 (0.60-0.62)
45-54 y	0.64 (0.63-0.65)	0.66 (0.65-0.67)	0.79 (0.78-0.81)	0.68 (0.67-0.69)	0.73 (0.72-0.74)	0.75 (0.74-0.77)	0.65 (0.64-0.66)
55-64 y	0.70 (0.69-0.71)	0.73 (0.71-0.75)	0.85 (0.83-0.87)	0.72 (0.71-0.74)	0.76 (0.75-0.78)	0.82 (0.81-0.84)	0.70 (0.68-0.71)
Women, mean (CI) for age groups:							
25-34 y	0.55 (0.55-0.56)	0.55 (0.55-0.56)	0.68 (0.67-0.68)	0.57 (0.57-0.58)	0.67 (0.66-0.68)	0.63 (0.62-0.64)	0.53 (0.52-0.54)
35-44 y	0.59 (0.58-0.59)	0.59 (0.58-0.60)	0.71 (0.70-0.72)	0.62 (0.61-0.62)	0.68 (0.67-0.68)	0.68 (0.67-0.69)	0.58 (0.57-0.58)
45-54 y	0.62 (0.62-0.63)	0.66 (0.65-0.67)	0.76 (0.74-0.77)	0.68 (0.67-0.69)	0.70 (0.69-0.71)	0.76 (0.75-0.78)	0.62 (0.61-0.64)
55-64 y	0.68 (0.67-0.69)	0.71 (0.69-0.72)	0.81 (0.80-0.82)	0.72 (0.71-0.73)	0.73 (0.72-0.75)	0.81 (0.80-0.83)	0.68 (0.67-0.69)
Presence of plaque on right or left carotid artery							
Prevalence, % (CI)	14.0 (11.8-16.2)	7.7 (6.1-9.2)	6.8 (5.5-8.1)	9.4 (7.8-10.9)	4.5 (3.3-5.7)	7.4 (6.0-8.8)	8.3 (6.9-9.6)

CI = confidence interval.

Table 4 Prevalences (as Percent and 95% Confidence Interval) of Risk Factor Associations

	Barquisimeto	Bogota	Buenos Aires	Lima	Mexico City	Quito	Santiago
Hypertension + Hypercholesterolemia	2.6 (1.9-3.3)	2.4 (1.8-3.1)	7.9 (6.8-9.1)	2.6 (1.9-3.2)	3.0 (2.2-3.7)	2.5 (1.8-3.1)	5.6 (4.5-6.8)
Hypertension + Diabetes	3.1 (2.4-3.8)	2.4 (1.7-3.2)	3.4 (2.4-4.5)	1.5 (0.9-2.0)	2.5 (1.9-3.2)	1.1 (0.7-1.5)	3.6 (2.7-4.6)
Hypertension + Smoking	3.5 (2.6-4.4)	1.8 (1.2-2.4)	9.3 (7.9-10.6)	3.4 (2.5-4.3)	1.7 (1.1-2.2)	2.4 (1.6-3.2)	7.9 (6.5-9.3)
Hypercholesterolemia + Diabetes	0.8 (0.4-1.1)	1.8 (1.2-2.5)	1.7 (1.0-2.3)	1.1 (0.5-1.6)	2.0 (1.3-2.7)	1.6 (1.0-2.1)	1.6 (1.0-2.3)
Hypercholesterolemia + Smoking	0.9 (0.5-1.3)	2.7 (2.0-3.5)	6.9 (5.6-8.2)	2.7 (2.0-3.5)	4.1 (3.2-5.0)	6.4 (4.8-7.9)	7.0 (5.7-8.4)
Diabetes + Smoking	0.9 (0.5-1.3)	1.9 (1.1-2.5)	2.3 (1.4-3.2)	1.2 (0.7-1.8)	2.5 (1.8-3.3)	1.4 (0.8-2.0)	2.8 (2.0-3.6)

Table 5 Prevalences (as Percent and 95% Confidence Interval) of Framingham Risk Score Categories

	Barquisimeto	Bogota	Buenos Aires	Lima	Mexico City	Quito	Santiago
Low (<10% 10-y risk)	88.6 (87.3-89.9)	84.8 (83.0-86.6)	82.9 (80.8-85.0)	86.7 (85.1-88.3)	85.5 (83.7-87.3)	83.2 (81.4-85.0)	82.0 (80.1-84.0)
Intermediate (10%-20% 10-y risk)	2.9 (2.3-3.5)	4.5 (3.6-5.4)	5.0 (3.9-6.1)	4.1 (3.2-5.0)	3.8 (2.9-4.6)	5.5 (4.5-6.6)	6.0 (4.9-7.0)
High (>20% 10-y risk)	8.5 (7.4-9.7)	10.7 (9.1-12.3)	12.1 (10.5-13.7)	9.2 (7.9-10.5)	10.7 (9.3-12.2)	11.2 (9.7-12.8)	12.0 (10.3-13.7)

CARMELA cities, the obesity/metabolic syndrome/diabetes trajectory differentially affects women. In Quito, the prevalence of obesity and diabetes in women is twice that in men; the ratio approaches 3:1 for metabolic syndrome. Buenos Aires was an exception to this trend, suggesting that local factors warrant research and intervention.

The tobacco epidemic has been divided into 4 stages on the basis of the prevalence of smoking and lung cancer deaths.[23] Stage I is the introduction of smoking into a population. In stage II, men's smoking rate increases to 50% to 80%, whereas women's smoking rate lags behind by 1 to 2 decades. Late in stage II, tobacco causes approximately 10% of men's deaths. During stage III, men's smoking rates decline and women's smoking rates peak, smoking-related mortality increases markedly, and antismoking policies begin. Stage IV sees a peak in female tobacco deaths early on with subsequent smoking rate declines in both sexes. In this stage, smoke-free workplaces become common, and eventually tobacco mortality decreases. The CARMELA data suggest that Santiago and Buenos Aires are in stage III, whereas other cities are in stage II. Women's lower rate of smoking in 5 of the 7 cities provides an opportunity for preventive measures. However, rates among women in Santiago and Buenos Aires are among the highest in the world.[24] Vigorous legislative measures, health care initiatives, and public awareness campaigns are required to decrease smoking.

Intima-media thickness measurements and carotid plaque noninvasively predict cardiovascular incidents, give an indication of atherosclerosis in progress,[10] and have been used as established outcome measures in interventional trials.[25] In the CARMELA cities, intima-media thickness and the prevalence of plaque varied widely, but the age effect on intima-media thickness was consistent with that in other countries.[26] CARMELA will contribute to defining the reference values and population distribution of intima-media thickness in the Latin American population.

The presence of multiple risk factors can greatly increase cardiovascular risk; for instance, hypertension plus hypercholesterolemia increases cardiovascular risk additively,[27] whereas hypertension plus diabetes exerts a multiplicative effect.[28] In the CARMELA cities, the prevalence of hypertension plus hypercholesterolemia ranged from 2% to 8% and the prevalence of hypertension plus diabetes ranged from 1% to 4%.

CONCLUSIONS

On the basis of the Framingham risk scores, 1 in 7 persons in the CARMELA cities is at significant risk for a cardiovascular event. Although the appropriateness of using the Framingham algorithm for non-US populations has not been demonstrated,[29] this algorithm may provide an initial heuristic for exploring risk patterns until a Latin American risk scoring system is developed and validated.

The CARMELA study is a large cross-sectional, observational study with the added value of being conducted mostly by practicing clinicians integrated in a continental network. The size of this study, the stratified multistage sampling method, and the rigorous design generated consistent estimates among the 7 cities, circumventing a major confounder in international risk comparisons—that of heterogeneity of age groups and other criteria across studies. Study limitations include its cross-sectional rather than longitudinal nature, exclusion of unsafe areas (which might have affected the socioeconomic balance of the sample), and exclusion of non-urban populations.

The INTERHEART study, a case-control study assessing the contribution of cardiovascular risk factors to the risk for acute myocardial infarction, showed that obesity, dyslipidemia, and smoking together account for 78% of the population-attributable risk in Latin America.[30] Epidemiologic data gathered in CARMELA complete the picture showing that the prevalence of these risk factors in major Latin American cities indicates the need for rational urban health policies. These data will help shape the Latin American response to the changing risk landscape accompanying the epidemiologic transition.

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References

1. Omran A. The epidemiologic transition: a theory of the epidemiology of population change. *Millbank Memorial Fund Q.* 1971;49:509-538.
2. Yusuf S, Reddy S, Ounpuu S, Anand S. Global burden of cardiovascular diseases: part I: general considerations, the epidemiologic transition, risk factors, and impact of urbanization. *Circulation.* 2001;104: 2746-2753.
3. World Health Organization. *The World Health Report: Reducing Risks, Promoting Healthy Life*. Geneva: World Health Organization; 2002.
4. Ordunez P, Silva LC, Rodriguez MP, Robles S. Prevalence estimates for hypertension in Latin America and the Caribbean: are they useful for surveillance? *Rev Panam Salud Publica.* 2001;10:226-231.
5. World Health Organization. *Preventing Chronic Diseases: A Vital Investment*. Geneva: World Health Organization; 2005.
6. Torres MI, Quiroga SE, Farinati ZJ. Pilot external quality assessment scheme for serology determinations in Latin America. *Clin Chem Lab Med*. Special Supplement 1999;37:S299.
7. Chobanian AV, Bakris GL, Black HR, et al. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7 report. *JAMA*. 2003; 289:2560-2572.
8. National Cholesterol Education Program Adult Treatment Panel III: Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. *Circulation.* 2002;106:3143-3421.
9. Expert Committee on the Diagnosis and Classification of Diabetes Mellitus: Report of the expert committee on the diagnosis and classification of diabetes mellitus. *Diabetes Care.* 2003;26(Suppl 1):S5-S20.
10. Touboul PJ, Hennerici MG, Meairs S, et al. Mannheim intima-media thickness consensus. *Cerebrovasc Dis.* 2004;18:346-349.
11. Kearney PM, Whelton M, Reynolds K, et al. Global burden of hypertension: analysis of worldwide data. *Lancet.* 2005;365:217-223.
12. Hajjar I, Kotchen TA. Trends in prevalence, awareness, treatment, and control of hypertension in the United States, 1988-2000. *JAMA*. 2003; 290:199-206.
13. Ford ES, Mokdad AH, Giles WH, Mensah GA. Serum total cholesterol concentrations and awareness, treatment, and control of hypercholesterolemia among US adults: findings from the National Health and Nutrition Examination Survey, 1999 to 2000. *Circulation.* 2003; 107:2185-2189.
14. World Health Organization. *Obesity: Preventing and Managing the Global Epidemic*. Geneva: World Health Organization; 2000.
15. Ford ES, Giles WH, Dietz WH. Prevalence of the metabolic syndrome among US adults: findings from the third National Health and Nutrition Examination Survey. *JAMA*. 2002;287:356-359.
16. Alberti KG, Zimmet P, Shaw J. Metabolic syndrome—a new worldwide definition. A Consensus Statement from the International Diabetes Federation. *Diabet Med.* 2006;23:469-480.
17. King H, Aubert RE, Herman WH. Global burden of diabetes, 1995-2025: prevalence, numerical estimates, and projections. *Diabetes Care*. 1998;21:1414-1431.
18. Must A, Spadano J, Coakley EH, et al. The disease burden associated with overweight and obesity. *JAMA*. 1999;282:1523-1529.
19. Ford ES. Risks for all-cause mortality, cardiovascular disease, and diabetes associated with the metabolic syndrome: a summary of the evidence. *Diabetes Care.* 2005;28:1769-1778.
20. Reddy KS, Yusuf S. Emerging epidemic of cardiovascular disease in developing countries. *Circulation.* 1998;97:596-601.
21. Ezzati M, Vander Hoorn S, Lawes CM, et al. Rethinking the "diseases of affluence" paradigm: global patterns of nutritional risks in relation to economic development. *PLoS Med.* 2005;2:e133.
22. United Nations Development Programme. *Human Development Report 2005 International Cooperation at a Crossroads: Aid, Trade and Security in an Unequal World*. New York: United Nations; 2005.
23. Lopez AD, Collishaw NE, Piha T. A descriptive model of the cigarette epidemic in developed countries. *Tob Control.* 1994;3:242-247.
24. World Conference on Tobacco or Health. *Tobacco Control Country Profiles*. American Cancer Society, World Health Organization, and International Union Against Cancer; 2003.
25. Bots ML. Carotid intima-media thickness as a surrogate marker for cardiovascular disease in intervention studies. *Curr Med Res Opin.* 2006;22:2181-2190.
26. Touboul PJ, Vicaut E, Labreuche J, et al. Design, baseline characteristics and carotid intima-media thickness reproducibility in the PARC study. *Cerebrovasc Dis.* 2005;19:57-63.
27. Castelli WP. Epidemiology of coronary heart disease: the Framingham study. *Am J Med.* 1984;76:4-12.
28. Stamler J. Established major coronary risk factors. In: Marmot M, Elliott P, ed. *Coronary Heart Disease: From Aetiology to Public Health*. Oxford University Press; 1992.
29. Brindle P, Emberson J, Lampe F, et al. Predictive accuracy of the Framingham coronary risk score in British men: prospective cohort study. *BMJ.* 2003;327:1267.
30. Lanas F, Avezum A, Bautista LE, et al. Risk factors for acute myocardial infarction in Latin America: the INTERHEART Latin American study. *Circulation.* 2007;115:1067-1074.