RIC

ARTÍCULO ORIGINAL

Applicability of the National Cholesterol Education Program III (NCEP-III) Guidelines for treatment of dyslipidemia in a non-Caucasian population: A Mexican Nation-Wide Survey

Rosalba Rojas,* Carlos A. Aguilar-Salinas,** Francisco J. Gómez-Pérez,**
Victoria Valles,** Aurora Franco,* Gustavo Olaiz,* Jaime Sepúlveda,* Juan A. Rull**

* Instituto Nacional de Salud Pública, Cuernavaca, Morelos.
** Departamento de Endocrinología y Metabolismo del Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán.

ABSTRACT

We assessed the impact of the NCEP-III recommendations in a population-based, nation-wide Mexican survey. Information was obtained from 15,607 subjects aged 20 to 69 years. In this report, only samples obtained after a 9 to 12 hours fast are included (2,201 cases). A cardiovascular risk equivalent was found in 10.5% and ≥ 2 risk factors were present in 41.7% of the population. In 10% of cases, the LDL-C concentration was high enough to be an indication for a lipid-lowering drug (> 160 mg/dL), independent of the presence of risk factors. A quarter of the population was eligible for some form of treatment (lifestyle modifications in 15.9%, drug therapy in an additional 11.7%). Among cases with ≥ 2 risk factors, a small percentage (1.8%) were identified as having a 10 year-risk > 20% and 86.3% were considered as having a10 year-risk < 10%. The majority of the metabolic syndrome cases (84%) were identified as low-risk subjects. As a result, only 17.6% of them qualified for drug-based LDL-C lowering. Our data helps to estimate of the magnitude of the burden imposed on the Mexican health system, of lowering LDL-C for cardiovascular prevention. If we apply our results to the 2,000 Mexican population census more than 5.8 million cases nationwide may require LDL lowering drug therapy following the NCEP-III criteria.

Key words. Cholesterol. Triglycerides. Mexico. Glucose intolerante. ATP-III.

Aplicabilidad del III Programa Nacional de Educación en Colesterol (NCEP-III). Guías para el tratamiento de la dislipidemia en una población no caucásica. Un estudio en toda la nación mexicana

RESUMEN

Evaluamos el impacto de las recomendaciones del Programa Nacional de Educación en Colesterol (NCEP-III) en muestra poblacional. La información proviene de 2,201 sujetos de 20 a 69 años cuyas muestras se obtuvieron después de un ayuno de 9 a 12 horas. Una condición con riesgo cardiovascular equivalente al de la cardiopatía isquémica se encontró en 10.5%; ≥ 2 factores de riesgo se encontraron en 41.7%. El colesterol LDL (LDL-C) fue suficientemente alto (> 160 mg/dL) para indicarse tratamiento hipolipemiante con medicamentos, en ausencia de otros factores de riesgo en 10% de los participantes. El 25% de la población calificó para recibir tratamiento hipolipemiante (cambios del estilo de vida 15.9% y tratamiento farmacológico en 11.7%). En casos con ≥ 2 factores de riesgo, un pequeño porcentaje (1.8%) fue identificado con riesgo mayor a > 20% de tener un evento cardiovascular a 10 años; 86.3% fue identificado con bajo riesgo (< 10% a 10 años). La mayoría de los casos con síndrome metabólico (84%) fueron identificados en el grupo de bajo riesgo. Como resultado, sólo 17.6% de ellos calificó para disminuir su LDL-C con medicamentos. Nuestros datos demuestran el reto que representa la prevención de complicaciones cardiovasculares por medio de la reducción de la concentración del LDL-C. Extrapolando nuestros datos al censo 2000, más de 5.8 millones de mexicanos califican para recibir tratamiento farmacológico de acuerdo con los criterios del NCEP-III.

Palabras clave. *Colesterol. Triglicéridos. México. Intolerancia a la glucosa. ATP-III.*

INTRODUCTION

Assessment of cardiovascular risk attributable to lipoprotein abnormalities is a controversial issue. Several parameters, cutoff points and algorithms have been used.[1-3] In 2001, a new version of the recommendations of the Expert Panel on Detection, Evaluation and Treatment of the National Cholesterol Education Program (NCEP III) was published.[4] This report introduces the concept of "equivalents of coronary heart disease" for conditions with similar event rates for cardiovascular mortality. It also includes a revised Framingham risk equation[5] for the estimation of the absolute cardiovascular risk. Finally, the low-density cholesterol (LDL-C) is considered the most important lipid parameter; the treatment eligibility LDL-C thresholds were lowered in some subsets of the population. The impact of this report was assessed in the Third Annual National Health and Nutrition Survey (NHANES III).[6] Here, patients younger than age 45 or older than age 65, especially males, were more likely to require treatment. The NCEP III recommendations are now routinely used in a number of countries. However, the lipid profile abnormalities differ between ethnic groups.[7] The mean LDL-C concentrations are significantly lower in Hispanic or Asian groups.[8,9] These subjects will require a greater number of cardiovascular risk factors in order to be eligible for treatment. As a consequence, the impact of the NCEP-III recommendations should also be assessed in non-Caucasian populations.

Between 1992-1993, the Mexican Ministry of Health conducted the National Survey of Chronic Diseases to estimate the prevalence of obesity, type 2 diabetes, renal pathology, hypertension and dyslipidemia. Using this population-based, nation-wide data, we describe the number and the characteristics of urban Mexican adults who are eligible for treatment using the NCEP-III recommendations.

MATERIAL AND METHODS

Population sample

This is a comparative, cross sectional study that includes individuals from cities with populations greater than 2,500 people. The characteristics of the population and the sampling procedure have been described elsewhere.[10-14] Briefly, a multistage sampling procedure was used. The country was divided in four regions (Northern, Central and Southern composed of 10 states each and the fourth region was comprised of the Metropolitan area of Mexico City and two states located in Central Mexico). A random sample of Basic Geographical Statistical Units was obtained in each state from a database generated by the Instituto Nacional de Geografía y Estadística; the Health Ministry constructed the general sampling frame. Neighborhood blocks were randomly selected and all adults (20 to 69 years) in every household of the selected blocks were surveyed with the exception of those living in military, religious, health and other institutions. A total of 417 cities were studied. The sample was representative of the Mexican urban population, which in 1990 constituted 71% of the total population.[15] A target of 4,731 individuals and 2,030 households per region was estimated using the household as the sampling unit with on average of 2.33 adults per household (according the 1990 National Census). Information was obtained in 15,607 subjects; the response rate was 82.5%. However, in this report, only the results of 2,201 subjects are included. These patients provided blood samples after a 9 to 12 h fast, required for the measurement of a complete lipid profile (15.3% of the population). Persons were invited to participate and instructed to remain fasted for 9 to 12 hours period the day scheduled for the visit. Several households were visited every day. However, the required fasting conditions were present only in the households visited at the beginning of every journey; it was by chance in which the order of the visits was performed. Cases were randomly distributed throughout the population; no bias was detected for age, gender, region or socioeconomic status. The study was realized in accordance with the Helsinki Declaration of Human Studies.

Personal interview

A structured interview was conducted. A previously standardized questionnaire was used to obtain information on demographic and socioeconomic aspects, family medical history, personal medical history, and lifestyle factors such as smoking. In the same visit, anthropometric and blood pressure measurements were obtained. Systolic (1st-phase) and diastolic (5th-phase) blood pressures were measured to the nearest even digit with a sphygmomanometer with the subject in the supine position after a 5 minutes rest. Blood pressure was measured twice in every case with an initial measurement of ≥ 120/80 mm Hg. The second measurement was done after a five minutes rest period in a seated position. The mean of these measurements was included in the database. The blood pressure was measured only once in the remaining cases.

Participants removed their shoes and upper garments. Height was measured to the nearest 0.5 cm. Body weight was measured on a daily calibrated balance and recorded to the nearest 0.1 kg. Body Mass Index (BMI) was calculated as weight (kg) divided by height (m^2) and was used as an index of overall adiposity. The equipment was regularly calibrated using reference samples provided by the manufacturer.

METHODS

All analytical measurements were done at the Departamento de Endocrinología and Metabolismo of the Instituto Nacional de Ciencias Médicas y Nutrición "Salvador Zubirán". The sampling procedure was standardized during a 28 weeks training course. The subjects were sampled in their homes; they remained seated for five minutes before the blood was drawn.

All samples were kept frozen at - 80 ºC until they were analyzed; the maximum time of storage was 12 months. Glucose was analyzed by the glucose-oxidase method (Boehringer Mannheim). Serum concentrations of total cholesterol and triglycerides were determined by enzymatic methods (Boehringer Mannheim). HDL-cholesterol was measured after precipitation of VLDL and LDL by the phosphotungstate method (Boehringer Mannheim), LDL-cholesterol was measured by an immunochemical direct method. Intra-assay CV values for total cholesterol, triglycerides and HDL-cholesterol were 3%, 5% and 5%, respectively. Our laboratory followed standardization procedures in accordance with the World Health Organization recommendations, including the use of external control sera.

Definitions

The NCEP III guidelines were applied to each subject. According to the NCEP III recommendations, patients with no coronary heart disease (CHD) or equivalent are considered elegible for treatment if they have ≤ 1 CHD risk factors and LDL-C ≥ 190 mg/dL or ≥ 2 CHD risk factors and LDL ≥ 160 mg/dL. For CHD patients or equivalent, treatment is considered neccesary if the LDL-C ≥ 130 mg/dL. Positive risk factors for CHD include age (≥ 45 years for men or ≥ 55 for women), family history of CHD, current cigarrette smoking, hypertension (blood pressure ≥ 140/90 mmHg or on antihypertensive medication) and low HDL-C (< 40 mg/dL). An HDL-C ≥ 60 mg/dL is considered a negative risk factor, allowing the removal of one point from the sum of risk factors. The selection criteria for treatment according to the NCEP III recommendations are shown in table I. The 10-year absolute risk was calculated with sex- and age-specific Framingham score sheets. The number of cases requiring lifestyle changes or drug therapy was calculated accordingly.

Family history of coronary heart disease was considered present based on reports by participants that a first-degree relative had a heart attack some time in their lives. Overweight was defined as BMI 25-30 kg/m^2 for males and females. Obesity was defined as BMI ≥ 30 kg/m^2. Individuals were classified as diabetics if they had a previous diagnosis of diabetes or had a fasting blood glucose value ≥ 7 mmol/L (126 mg/dL) with no previous history of diabetes. Hypertension was defined as a systolic pressure ≥ 140 mm Hg and/or diastolic pressure ≥ 90 mm Hg and/or current use of antihypertensive medications. Ischemic heart disease was considered if there was a history of myocardial infarction. Smoking was defined as any tobacco consumption during the month previous to sampling. The metabolic syndrome was diagnosed using the NCEP criteria.[4,12] A body mass index > 30 kg/m^2 was used intead of the NCEP waist circumference criteria because this parameter was not measured in our survey.

Table 1. National Cholesterol Education Program-III treatment recommendations.

- Eligibility for drug treatment under NCEP-III
- Coronary heart disease (CHD) or an equivalent condition (diabetes, stroke, arterial insufficiency of the lower limbs) and LDL cholesterol ≥ 130 mg/dL (goal LDL cholesterol < 100 mg/dL).
- ≥ 2 cardiovascular risk factors* and a 10-year risk of CHD > 20% and LDL cholesterol ≥ 130 mg/dL (goal LDL cholesterol < 100 mg/dL)
- ≥ 2 cardiovascular risk factors* and a 10-year risk of CHD 10- 20% and LDL cholesterol ≥ 130 mg/dL (goal LDL cholesterol < 130 mg/dL)
- ≥ 2 cardiovascular risk factors* and a 10-year risk of CHD < 10% and LDL cholesterol ≥ 160 mg/dL (goal LDL cholesterol < 130 mg/dL)
- < 2 cardiovascular risk factors* and LDL cholesterol ≥ 190 mg/dL (goal LDL cholesterol < 160 mg/dL)

Positive risk factors include age (≥ 45 years for men, ≥ 55 years for women), family history of premature CHD (CHD in male first-degree relative < 55 years; CHD in female first-degree relative < 65 years), current cigarette smoking, hypertension or anti-hypertensive treatment and low HDL cholesterol (< 40 mg/d). High HDL cholesterol (≥ 60 mg/dL) is a negative risk factor; a positive risk factor is removed from the total count by its presence.

Statistical analysis

The data were coded and captured under ASCII fixed format. The database was validated through recognition of missing values, outliers and inconsistencies between variables. Descriptive analysis included the estimation of mean values and standard deviations for continuous variables. These values were rounded to the nearest integer or first decimal point. Prevalence and frequencies are expressed in term of percentage. Significance of the differences between the subgroups was tested by one-way ANOVA using Scheffé's multiple comparison method. Categorical variables were compared by the chi square statistic with Yates' correction or the exact Fisher test when appropriate. All the statistical analysis was conducted using the SAS statistical package (SAS Institute).

RESULTS

In this analysis, 2201 cases were studied. The population was composed mainly of subjects younger than 40 years; the age and gender distribution was representative of the Mexican adults (Table 2). Mean lipid concentrations were cholesterol 182.7 ± 40 mg/dL, triglycerides 213.4 ± 158 mg/dL, HDL-C 38.3 ± 9.5 mg/dL and LDL-C 116.4 ± 36 mg/dL. The BMI was 27.09 ± 5.6 kg/m^2. In agreement with a previous report carried out in the same population,[10] several cardiovascular risk factors were common. Diabetes, high blood pressure and obesity were found in 6.1, 21.88 and 20 percent of the subjects, respectively. Smoking was reported in 28% and almost half the population (46%) had primary school education or less.

A coronary heart disease equivalent was found in 10.5% of the subjects. Two or more risk factors were found in 41.7% of the population. Thus, independent of the LDL-C concentration, almost half of the Mexican adults living in an urban area are potential candidates for intensive lipid-lowering therapy. The distribution of the LDL-C concentrations, stratified by the thresholds proposed by the NCEP-III report, is shown in table 3. The LDL-C concentration was high enough to be a potential indication of a lipid-lowering drug therapy (> 160 mg/dL), independent of other risk factors, in 10% of the popu-

Table 2. Distribution of all treatment eligible patients stratified by age and gender group in the Mexican National Survey of Chronic Diseases and its comparison against the Third Annual National Health and Nutrition Survey (NHANES III).

Age range (y)	Mexican survey of chronic disease			NHANES III
Total [n (%)]	LSM	Drug therapy	Total	Drug therapy (%)
20-29 (n = 866)	71(8.1)	23 (2.6)	94 (10.8)	6.3
30-39 (n = 579)	86 (14.8)	55 (9.5)	141 (24.3)	13.2
40-49 (n = 373)	86 (23.1)	53 (14.2)	139 (37.3)	16.9
50-59 (n = 239)	62 (25.9)	78 (32.6)	140 (58.6)	24.4
60-69 (n = 144)	46 (31.9)	49 (34.0)	95 (65.9)	38.2
Total (n = 2201)	351 (15.94)	258 (11.7)	609 (27.6)	17.5
Males [n (%)]				
20-29 (n = 380)	42 (11.1)	18 (4.7)	60 (15.8)	6.1
30-39 (n = 233)	39 (16.7)	36 (15.4)	75 (32.2)	17.8
40-49 (n = 158)	47 (29.7)	29 (18.3)	76 (48.1)	21.1
50-59 (n = 96)	19 (19.8)	45 (46.8)	64 (66.7)	28.3
60-69 (n = 63)	23 (36.5)	22 (34.9)	45 (71.4)	42.1
Subtotal (n = 930)	170 (18.3)	150 (16.1)	320 (34.4)	20.4
Females [n (%)]				
20-29 (n = 486)	29 (5.9)	5 (1.0)	34 (7.0)	6.7
30-39 (n = 346)	47 (13.5)	19 (5.5)	66 (19.1)	8.7
40-49 (n = 215)	39 (18.1)	24 (11.2)	63 (29.3)	12.9
50-59 (n = 143)	43 (30.1)	33 (23.1)	76 (35.3)	20.6
60-69 (n = 81)	23 (28.4)	27 (33.3)	50 (61.7)	34.8
Subtotal (n = 1271)	181(14.2)	108 (8.5)	289 (22.7)	14.6

Data of the NHANES III were obtained from references 6 and 21. LSM = Lifestile modification.

Table 3. Percent of patients with increased low density lipoprotein cholesterol (LDL-C) concentrations in the study subjects stratified according to the presence of coronary heart disease or cardiovascular risk factors (n = 2,201).

	LDL- C (mg/dL)					
Strata [n (% between group)]	< 100	100-130	130-160	160-190	> 190	No data available
Coronary heart disease or diabetes [n= 231 (10.5 %)]	53(22.9)	80 (34.6)	56 (24.2)	29 (12.5)	8 (3.4)	5(2.2)
CHD, stroke or arterial insufficiency in lower Limbs (n = 37)	11 (29.7)	11 (29.7)	11 (29.7)	4 (10.8)	0(0)	0(0)
Diabetes (n = 194)	42 (21.7)	69 (35.6)	45 (23.2)	25 (12.9)	8 (4.1)	5 (2.6)
Without CHD						
Two or more risk factors [n = 919 (41.7%)]						
10 year risk > 20 (n = 17)	1 (5.8)	2 (11.7)	8 (47.1)	3 (17.6)	3 (17.6)	0(0)
10 year risk 10-20% (n = 109)	16 (14.6)	31 (28.4)	33 (30.3)	15 (13.7)	10 (9.2)	4(3.7)
10 year risk < 10% (n = 793)	257 (32.4)	274 (34.5)	177 (22.3)	58 (7.3)	20 (2.5)	7 (0.9)
One risk factor [n = 705 (32.0%)]	282 (40.0)	227 (32.2)	140 (19.9)	40 (5.7)	9 (1.3)	7 (1.0)
No risk factor (n = 346 (15.7%))	170 (49.1)	97 (28.0)	51 (14.7)	20 (5.8)	6 (1.7)	2 (0.5)
Total	779 (35.4)	711 (32.3)	465 (21.1)	165 (7.5)	56 (2.5)	25 (1.1)

Table 4. Distribution of treatment eligible patients (n = 2,201).

	LSM	Drug therapy
Strata [n (% between group)]		
Coronary heart disease or diabetes [n = 231 (10.5 %)]		
CHD, stroke, arterial insufficiency in lower limbs (n = 37)	11 (29.7)	15 (40.5)
Diabetes (n = 194)	69 (35.6)	78 (40.2)
Without CHD		
Two or more risk factors [n = 919 (41.7%)]		
10 year risk > 20 (n = 17)	2 (11.8)	14 (82.4)
10 year risk 10-20% (n = 109)	31 (28.4)	58 (53.2)
10 year risk < 10% (n = 793)	177 (22.3)	78 (9.8)
One risk factor [n = 705 (32.0%)]	20 (2.8)	9 (1.2)
No risk factor [n = 346 (15.7%)]	40 (11.5)	6 (1.7)
Total	350 (15.9)	258 (11.7)

LSM = Lifestyle modifications.

lation (n = 221). Thus, the majority of cases that qualifies for drug treatment does it because they have moderate hypercholesterolemia and coexisting co-morbidities that increase their cardiovascular.

The percentage of cases that qualified for treatment according the NCEP III report is shown in table 4. A quarter of the population was found to be eligible. Lifestyle modifications were the core of the therapy in 15.9% of the cases; the addition of drug therapy was required in an additional 11.7%. The distribution of eligible patients according to age and gender is shown in table 2. Among those only requiring lifestyle modifications, 48.4% were males, 44.7% were younger than age 40 and 13% were older than age 60. For cases that also required drug treatment, 58.1% were males, 30.2% were younger than age 40 years and 18.9% were older than age 60.

As expected, the percentage of cases that required some form of treatment was significantly greater in cases with coronary heart disease or an equivalent condition (lifestyle modification 34.6% and drug therapy 40.25%). These rates are in contrast with the small percentages found in cases with one or less risk factors (lifestyle changes 5.7%, drug therapy 1.4%). Thus, the NCEP-III approach directs the intervention to the cases with the highest risk.

The group with two or more risk factors deserves special attention. The distribution of the NCEP risk factors by age group is shown in table 5. The most frequent risk factor was a low HDL cholesterol concentration; it was present in 786 (85.5%) of the 919 subjects of this group. The coexistence of smoking was the most common combination among young adults (< 40 years). In contrast, the coexistence of arterial hypertension was the most frequent finding in cases older than age 40. The use of the Framingham tables is limited to the group with two or more risk factors. Based on the risk score evaluation, the LDL-C goal is selected. A small percentage (1.8%) was identified as high-risk (10 year risk > 20%); almost every case in this group qualified for drug therapy. In contrast, 86.3% of the cases with 2 or more risk factors were identified as low risk individuals (10 year risk< 10%): only a few (9.8%) qualified for drug therapy. Thus, the use of the Framingham tables has a large impact on the proportion of cases with 2 or more risk factors that qualify for drug therapy.

The validation of the Framingham tables has been done mainly in Caucasian subjects. Since the use of this instrument has a remarkable impact on the selection of cases that qualify for drug treatment, we evaluated the differences between subjects stratified into the three categories of the Framingham tables. As shown in table 6, cases with the highest risk (a 10 year risk > 20%) were the oldest, had the highest prevalence of high blood pressure and the highest levels of LDL-C and non-HDL cholesterol. However, the cases with lower risk (10 year risk < 10%) had a similar prevalence of obesity and their mean HDL-C concentration was no different from that found in the high-risk subjects. Thus, the prevalence of some conditions (e.g. several components the metabolic syndrome) not taken into account by the Framingham tables (i.e. obesity) is similar among cases identified as high or low risk.

A separate analysis was performed in the non-diabetic cases with metabolic syndrome (n = 408). Less than 2 NCEP-III risk factors were present in 99 ca-

Table 5. Contribution of the National Cholesterol Education Program risk factors in the group with two or more risk factors.

Age group (years)	HDL < 40 mg n (%)	Arterial hypertension n (%)	Smoking n (%)	Family history n (%)	Men ≥ 45 y n (%)	Women ≥ 55 y n (%)
20-29 (n = 293)	267 (91.1)	117 (39.9)	124 (42.5)	71(24.3)	-	-
30-39 (n = 223)	210 (94.2)	91 (40.8)	94 (42.1)	72 (32.3)	-	-
40-49 (n = 187)	159 (85)	104 (55.6)	73 (39.3)	52 (27.8)	62 (33.2)	-
50-59 (n = 132)	104 (78.8)	69 (52.3)	44 (33.3)	41 (31.1)	69 (52.3)	31 (23.5)
60-69 (n = 84)	46 (54.8)	61 (72.6)	23 (27.4)	18 (21.4)	39 (46.4)	45 (53.6)
Total (n = 919)	786 (85.5)	442 (48.1)	359 (39.1)	254 (27.6)	170 (18.5)	76 (8.3)

Table 6. Characteristics of the study subjects without coronary heart disease with ≥ 2 risk factors that qualified or not for drug therapy based on the results of the Framingham tables.

10ys risk	< 10%	10- 20%	> 20%	p value
N =	793	109	17	
Age	36.2 ± 12	53.2 ± 9	56.3 ± 7	< 0.001
Body mass index (kg/m^2)	26.9 ± 5	27.7 ± 5	26.5 ± 5	0.34
Obesity [n (%)]	180(22.9)	28(25.7)	3(17.6)	0.87
Systolic pressure (mm Hg)	131 ± 17	141 ± 19	148 ± 17	< 0.001
Diastolic pressure (mm Hg)	87 ± 14	91 ± 14	92 ± 12	< 0.001
High blood pressure [n (%)]	325(41)	62(57)	12(71)	< 0.001
HbA1 (%)	7.8 ± 1.4	8.1 ± 1.2	7.8 ± 2	0.16
Glucose (mg/dL)	91.2 ± 11.8	95.2 ± 10.9	98.5 ± 14	< 0.001
Cholesterol (mg/dL)	177 ± 38	206 ± 39	234 ± 39	< 0.001
HDL-Cholesterol (mg/dL)	34 ± 8	33 ± 8	35 ± 7	0.34
LDL-Cholesterol (mg/dL)	116 ± 34	139 ± 41	163 ± 41	< 0.001
Non-HDL cholesterol (mg/dL)	143 ± 38	173 ± 39	199 ± 38	< 0.001
Triglycerides (mg/dL)	173 ± 123	227 ± 120	234 ± 101	< 0.001
Metabolic syndrome [n (%)]	245(32)	54(49.5)	8(47)	< 0.001

Table 7. Distribution of treatment eligible patients based on their non-HDL cholesterol stratified according to the presence of coronary heart disease or cardiovascular risk factors (n = 2,201).

	Non HDL- C (mg/dL)					
Strata [n (% between group)]	< 100	100-130	130-160	160-190	> 190	No data available
Coronary heart disease						
or diabetes [n= 231 (10.5 %)]	9(3.9)	46 (19.9)	69 (29.8)	57 (24.6)	48 (20.8)	2 (0.8)
CHD, stroke or arterial insufficiency in lower						
Limbs (n = 37)	3 (8.1)	12 (38.7)	9 (24.3)	8 (25.8)	5 (13.5)	0(0)
Diabetes (n = 194)	6 (3.1)	34 (17.5)	60 (30.9)	49 (25.2)	43 (22.2)	2 (1.0)
Without CHD						
Two or more risk factors [n = 919 (41.7%)]						
10 year risk > 20 (n = 17)	0 (0)	0 (0)	3 (17.7)	5 (29.4)	9 (52.9)	0 (0)
10 year risk 10-20% (n = 109)	1 (0.9)	10 (9.2)	28 (25.7)	42 (38.5)	28 (25.7)	0 (0)
10 year risk < 10% (n = 793)	91 (11.5)	218 (27.5)	239 (30.1)	167 (21.1)	78 (9.8)	0 (0)
One risk factor [n = 705 (32.0%)]	128 (18.2)	217 (30.8)	199 (28.2)	116 (16.5)	45 (6.4)	0(0)
No risk factor [n = 346 (15.7%)]	87 (25.1)	124 (35.8)	77 (22.2)	40 (11.5)	18 (5.2)	0 (0)
Total	316 (14.4)	615 (27.9)	615 (27.9)	427 (19.4)	226 (10.3)	2(0.09)

ses (24.3%). Of these, only 12 subjects had an LDL-C > 160 mg/dL (the LDL-C threshold for receiving any form of lipid-lowering treatment). In the remaining 309 cases (75.7%), two or more risk factors were present. In the majority of this subgroup, the estimated 10-year risk was < 10% (79.28%); as a result, the LDL-C threshold for drug therapy becomes higher (≥ 160 mg/dL) in this group. Thus, in spite of the well-known cardiovascular risk of the metabolic syndrome,[8] only a small proportion of cases qualified for drug therapy (23% among cases with ≥ 2 risk factors, and 17.6% among all the non-diabetic cases with metabolic syndrome).

Because of the high prevalence of hypertriglyceridemia in our population, we assessed the effects of using the non-HDL cholesterol instead of the LDL cholesterol as the prime goal of therapy.[16-18] The results are shown in table 7. The number of cases that qualifies for receiving treatment was not modified; this was true for all three cardiovascular risk categories shown in table 7. For example, among the patients with diabetes, (the group in which the LDL-C is most likely to be underestimated), the number of cases that have the recommended LDL-C or non HDL-C was almost the same (42 for LDL-C < 100 mg/dL and 40 for non HDL-C < 130 mg/dL).

DISCUSSION

The NCEP III recommendations are the standard of care for dyslipidemic cases in many countries. Their implementation is supported by prospective data derived mainly from Caucasian groups. However, these criteria are widely used in non-Caucasian populations, despite the fact that these populations have a differing prevalence of several types of dyslipidemia. Thus, the ability to identify and treat patients with increased cardiovascular risk must be measured in population-based studies of non-Caucasian subjects. In this survey, representative of urban Mexican adults aged 20 to 69 years, a coronary heart disease equivalent was found in 10.5% and two or more risk factors were detected in an additional 41.7%. Nearly a quarter of the study population qualified for some form of lipid lowering therapy: LDL-C lowering drug treatment was recommended for 11.7%. Our data helps to estimate the magnitude of the burden imposed on the Mexican health system of lowering LDL-C for cardiovascular prevention. Applying our results to the 2000 Mexican population census[19] (considering only the segment of the population covered by our survey), more than 5.8 million cases nationwide may require LDL lowering drug therapy following the NCEP-III criteria.

The NCEP-III approach directs intervention to the cases with the highest risk.[20] The percentage of cases that qualified for drug therapy was proportional with increasing age, in the high-risk groups, and in males (Tables 2 and 4). For example, the percentage was significantly greater in cases with coronary heart disease or equivalent condition (lifestyle modification 34.6% and drug therapy 40.25%) compared with that

found in cases with one or less risk factors (lifestyle changes 5.7%, drug therapy 1.4%). An LDL-C < 100 mg/dL was the target of treatment in 11.2% of Mexican adults; some form of lipid-lowering treatment would be needed in 78.2% of these to reach this goal. A significant proportion (29%) of the total number of cases that qualified for drug therapy was younger than age 40. This fact is explained by the age distribution of the Mexican population, composed mainly of young adults. These data clearly reflect the magnitude of the challenge that the treatment of hypercholesterolemia represents for the Mexican society.

The proportion of cases eligible for treatment in our population was compared with data reported in the United States. Differences in the age range covered and in the distribution of the age groups between our survey and the NHANES-III report[6] limit a direct comparison between these studies. Our analysis is, therefore, limited to the age groups examined in both studies (Table 2). In the US, 30.7 million people (17.5% of a population composed of 175.5 million inhabitants aged 20-69[21]) are eligible for LDL lowering by drug therapy; of these, 25.2% will have a LDL-C < 100 mg/dL as a treatment target.[6] Differences in the age distribution of the participants of these surveys explain the higher prevalence found in US adults. As shown in table 2, the percentages are very similar when subjects of the same age and gender group are compared. In addition, the prevalence of cases qualifying for drug therapy in our survey became similar to that found in the US, when our data were adjusted for the NHANES-III age and gender distribution (16.86% in our report *vs.* 17.5% in the US). Thus, the numbers of cases that may require lipid-lowering treatment may be even greater in the future, as the age distribution of the Mexican population continue to acquire the shape observed in more industrialized societies.[22]

The use of the Framingham tables, as proposed by the NCEP-III report, attempts to better identify the high-risk cases in the subject with 2 or more risk factors. Concerns have been expressed in non-Caucasian populations because the score overestimates the risk in these ethnic groups.[23-26] In our survey, only 13.7% of the ≥ 2 risk factors group was identified as having a 10 year-risk of CHD above 10%. This small percentage is explained by the age distribution of our population; a large proportion of the estimated risk depends on the subject's age. Thus, the possible overestimation of risk is counterbalanced by the age distribution of our population.

We assessed the differences between the cases with a 10 year-risk above 10% compared with other subjects with ≥ 2 risk factors with a 10 year risk lower than 10%. Age and cholesterol levels were the major differences observed (Table 5). A large percent of the metabolic syndrome cases were considered in the low-risk group. Therefore, few qualified for treatment (17.6% among the non-diabetic cases with metabolic syndrome). This observation contrasts with the well-described risk for coronary events in the metabolic syndrome (2.7 (95CI% 1.2-6.2%)).[27] In absolute terms, the metabolic syndrome represents a 10-year cardiovascular risk of 10-20%.[28] One of the explanations for this discrepancy is the use of the Framingham tables. In the Quebec study and post hoc analysis of similar investigations, these tables have proven to underestimate the risk associated with the metabolic syndrome.[29,30] This is probably because this instrument does not take into account the mechanisms by which the metabolic syndrome favors atherosclerosis progression. In our report, an additional 26.8% of the metabolic syndrome cases may qualified for drug therapy based on their LDL-C (130-160 mg/dL) if a 10 year risk of 10-20% is considered, instead of that estimated using Framingham score (< 10%). Hence, we strongly believe, as others[31] that the use of the Framingham tables should be reconsidered in the metabolic syndrome

Strengths and limitations must be recognized. The National Survey of Chronic Disease is the only representative population-based, nation-wide survey available in the Mexican population, in which the impact of the National Cholesterol Education Program-III can be assessed. Other surveys have not included a fasting lipid profile[32,33] in the evaluation. However, the percentages reported may have changed since the survey was performed. The body mass index was used instead of the waist circumference for the diagnosis of the metabolic syndrome; this limitation is shared with other population-based surveys.[34] Cardiovascular disease was diagnosed by self-report; this approach may result in underestimation of the prevalence. Family history of coronary heart disease was considered present based on reports by participants that a first-degree relative had a heart attack some time in their lives. Finally, there is no information about other relevant variables for the estimation of cardiovascular risk (e.g. physical activity and mental stress).

REFERENCES

1. Frohlich J, Fodor G, McPherson R, Genest J, Langer N for the Dyslipidemia Working Group of Health Canada. *Can J Cardiol* 1998; 14(Suppl. A): 17A-21A.

2. British Cardiac Society, British Hyperlipidemia Association, British Hypertension Society, British Diabetic Association. Joint British recommendations on prevention of coronary heart disease in clinical practice: summary. *BMJ* 2000; 320: 705-8.
3. American College of Physicians. Guidelines for using serum cholesterol, high density lipoprotein cholesterol and triglycerides levels as screening tests for preventing coronary heart disease in adults. Part 1. *Ann Intern Med* 1996; 124: 515-17.
4. Expert panel on detection, evaluation and treatment of high blood cholesterol in adults. Executive summary of the third report of the National Cholesterol Education Program (NCEP) Expert panel on detection, evaluation and treatment of high cholesterol. *JAMA* 2001; 285: 2486-97.
5. Grundy SM, Pasternak R, Greenland P, Smith S, Fuster V. Assessment of cardiovascular risk by use of multiple risk factor assessment equations. *Circulation* 1999; 100; 1481-92.
6. Fedder D, Koro C, L'Italien G. New National Cholesterol Education Program III guidelines for primary prevention lipid-lowering drug therapy. *Circulation* 2002; 105: 152-6.
7. Rodriguez C, Pablos-Méndez A, Palmas W, Lantigua R, Mayeux R, Berglund L. Comparison of modifiable determinants of lipids and lipoprotein levels among African-Americans, Hispanics and non-Hispanic Caucasians ≥ 65 years of age living in New York City. *Am J Cardiol* 2002; 89: 178-83.
8. Mitchell BD, Gonzalez Villalpando C, Arredondo Perez B, Garcia MS, Valdez R, Stern MP. Myocardial infarction and cardiovascular risk factors in Mexico City and San Antonio, Texas. *Arterioscler Thromb Vasc Biol* 1995; 15: 721-5.
9. Bhopal R, Unwin N, White M, Yallop J, Walker L, Alberti KGMM, Harland J, Patel S, Ahmad N, Turner C, Watson B, Kaur D, Kulkarni A, Laker M, Tavridou A. Heterogeneity of coronary heart disease risk factors in Indian, Pakistani, Bangladesh, and European origin populations: cross sectional study. *BMJ* 1999; 319: 215-20.
10. Aguilar-Salinas CA, Olaiz G, Valles V, Ríos JM, Gómez Pérez FJ, Rull JA, Rojas R, Franco A, Sepúlveda J. High prevalence of low HDL cholesterol concentrations and mixed hyperlipidemia in a Mexican nation wide survey. *J Lipid Research* 2001; 42: 1298-307.
11. Aguilar-Salinas CA, Rojas R, Gómez-Pérez FJ, García E, Valles V, Ríos-Torres JM, Franco A, Olaiz G, Sepúlveda J, Rull JA. Early onset type 2 diabetes in a Mexican, population-based, nation-wide survey: *Am J Med* 2002; 113: 569-74.
12. Aguilar-Salinas CA, Rojas R, Gómez-Pérez FJ, Valles V, Ríos-Torres JM, Franco A, Olaiz G, Rull JA, Sepulveda J. High prevalence of the metabolic syndrome in Mexico. *Arch Med Res* 2004; 35: 76-81.
13. Valles V, Aguilar-Salinas CA, Gómez-Pérez FJ, Rojas R, Franco A, Olaiz G, Rull JA, Sepúlveda J. Apolipoprotein B and AI distribution in the Mexican urban adults: Results of a Nation-Wide Survey. *Metabolism* 2002; 51: 560-8.
14. Aguilar Salinas CA, Rojas R, Gómez-Pérez FJ, Valles V, Ríos-Torres JM, Franco A, Olaiz G, Rull JA , Sepulveda J. Analysis of the agreement between the World Health Organization criteria and the National Cholesterol Education Program Definition of the metabolic syndrome (short report). *Diabetes Care* 2003; 26: 1635.
15. Instituto Nacional de Geografía y Estadística. Censo Nacional de Población 1990.
16. Aguilar-Salinas CA, Delgado A, Gómez-Pérez FJ. The advantages of using non-HDL cholesterol in the diagnosis and treatment of dislipidemias (letter). *Arch Intern Med* 2002; 162: 102-6.
17. Frost P, Havel R. Rationale for use of non high density lipoprotein cholesterol rather than low density lipoprotein cholesterol as a tool for lipoprotein cholesterol screening and assessment of risk and therapy. *Am J Cardiol* 1998; 81: 26B-31B.
18. Friedewald WT, Levy IR, Fredrickson DS. Estimation of the concentration of low density lipoproteins cholesterol in plasma without the use of the ultracentrifuge. *Clin Chem* 1972; 18: 449–502.
19. 2000 Mexican population census. Available at: www.inegi.gob.mx. Accessed April 12, 2002.
20. Gotto A, Kuller L. Eligibility for lipid-lowering drug therapy in primary prevention: How do the Adult Treatment Panel II and the Adult Treatment Panel III guidelines compare? *Circulation* 2002; 105: 136-9.
21. 2000 US population census. Available at: www.censusscope.org. Accessed September 20, 2004.
22. World Health Organization. Surveillance of risk factors related to noncommunicable diseases: current status of global data (SURF report). Available at: www.who.int/ncd/surveillance/surveillance_publications.htm. Accessed September 20, 2004.
23. Cappuccio F, Oakeshott P, Strazzullo P, Kerry S. Application of Framingham risk estimates to ethnic minorities in United Kingdom and implications for primary prevention of heart disease in general practice: cross sectional population based study. *BMJ* 2002; 1271-7.
24. Grundy SM, D'Agostino R, Mosca L, Burke G, Wilson P, Rader D, Cleeman J, Roccella E, Cutler J, Friedman L. Cardiovascular risk assessment based on US cohort studies: findings from a National Heart, Lung and Blood Institute Workshop. *Circulation* 2001; 104: 491-6.
25. Liu J, Hong Y, D'Agostino R, Wu Z, Wang W, Sun J, Wilson P, Kannel W, Zhao D. Predictive value for the Chinese population of the Framingham CHD risk assessment tool compared with Chinese multi-provincial cohort study. *JAMA* 2004; 291: 2591-9.
26. D'Agostino R, Grundy SM, Sullivan L, Wilson P for the CHD risk prediction group. Validation of the Framingham coronary heart disease prediction scores: Results of a multiple ethnic groups investigation. *JAMA* 2001; 286: 180-7.
27. Klein B, Klein R, Lee K. Components of the metabolic syndrome and risk of cardiovascular disease and diabetes in Beaver Dam. *Diabetes Care* 2002; 25: 1790-4.
28. Malik S, Wong N, Franklin S, Kamath T, L'Italien G, Pio J, Williams R. Impact of the metabolic syndrome on mortality from coronary heart disease, cardiovascular disease and all causes in United States adults. *Circulation* 2004; 110: 1245-50.
29. Girman C, Rhodes T, Mercuri M et al. The metabolic syndrome and risk of major coronary events in the Scandinavian Simvastatin Survival Study (4S) and the Air Force/Texas Coronary Atherosclerosis Prevention Study (AFCAPS/TexCAPS). *Am J Cardiol* 2004; 93: 136-41.
30. Despres JP, Lemieux I, Dagenais GR et al. Evaluation and management of atherogenic dyslipidemia: beyond low-density lipoprotein cholesterol. *CMAJ* 2001; 13: 1331-3.
31. Jacobson TA, Case CC, Roberts S, Buckley A, Murtaugh KM, Sung JC, Gause D, Varas C, Ballantyne CM. Characteristics of US adults with the metabolic syndrome and therapeutic complications. *Diabetes Obes Metab* 2004; 6: 353-62.
32. Sánchez-Castillo CP, Velázquez-Monroy O, Berber A, Lara-Esqueda A. Tapia-Conyer R, James PT and the Encuesta Nacional de Salud (ENSA) 2000 Working Group. Anthropometric cutoff points for predicting chronic diseases in the Mexican National Health Survey 2000. *Obesity Res* 2003; 11: 442-51.
33. Aguilar-Salinas CA, Vazquez-Chavez C, Gamboa-Marrufo R, García Soto N, Ríos Gonzalez JJ, Holguín R, Vela S, Ruiz Alvarez F, Mayagoitia S. Prevalence of obesity, diabetes, hypertension and tobacco consumption in an urban adult Mexican population. *Arch Med Res* 2001; 32: 446-53.

34. Ford E, Giles W, Dietz W. Prevalence of the metabolic syndrome among US adults. *JAMA* 2002; 287: 356-9.

Correspondence and reprint request:

Carlos Alberto Aguilar-Salinas, MD
Instituto Nacional de Ciencias Médicas y Nutrición
Salvador Zubirán
Vasco de Quiroga No. 15
14000, México, D.F.
Phone: 52-5-5133891
Fax: 52-5-5130002
E-mail: caguilarsalinas@yahoo.com

Recibido el 10 de junio de 2004.
Aceptado el 22 de noviembre de 2004.