Prevention of cardiovascular disease based on lipid lowering treatment: a challenge for the Mexican health system

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Abstract

Objective. To estimate the percentage of Mexican adults that may require lipid-lowering treatment according to National Cholesterol Education Program-III guidelines, using data from the National Health and Nutrition Survey 2006 (ENSANUT 2006). **Material and Methods.** Information was obtained from 4 040 subjects aged 20 to 69 years, studied after a 9 to 12 hours fast. **Results.** A cardiovascular risk equivalent was found in 13.8% and ≥2 risk factors were present in 31.5% of the population. LDL-C concentrations were above the treatment goal in 70% of the high-risk group and in 38.6% of subjects with ≥2 risk factors. Nearly 12 million Mexicans should be taught how to change their lifestyles and close to 8 million individuals require drug therapy to decrease their cardiovascular risk. **Conclusions.** Thirty percent of Mexican adults require some form of lipid-lowering treatment (lifestyle modifications in 36.25%, drug therapy in 24.19%).

Key words: cholesterol; triglycerides; cholesterol, HDL; LDL; hypercholesterolemia; hypoalphalipoproteinemia; Mexico

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Resumen

Objetivo. Calcular el porcentaje de adultos que requiere tratamiento hipolipemiante de acuerdo con las recomendaciones del Programa Nacional de Educación en Colesterol-III, usando los datos de la Encuesta Nacional de Salud y Nutrición 2006. **Material y métodos.** Se incluyeron 4 040 individuos con edad entre 20 y 69 años estudiados bajo un ayuno de 9 a 12 horas. **Resultados.** Un equivalente de enfermedad cardiovascular fue identificado en 13.8% de los participantes. El 31.5% de la población tenía ≥2 factores de riesgo cardiovascular. La concentración de colesterol LDL estuvo arriba de la meta terapéutica en 70% de los casos con alto riesgo cardiovascular y en el 38.6% de los sujetos con ≥2 factores de riesgo. Cerca de 12 millones de mexicanos deben modificar su estilo de vida para reducir su concentración de colesterol LDL. Casi 8 millones califican para recibir tratamiento farmacológico. **Conclusiones.** Una tercera parte de los adultos requiere alguna forma de tratamiento hipolipemiante (cambios en el estilo de vida: 36.25%, medicamentos: 24.19%).

Palabras clave: colesterol; triglicéridos; colesterol HDL; colesterol LDL; hipercolesterolemia; hipoalfalipoproteinemia; México

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Coronary heart disease (CHD) prevention programs heavily depend on the proper detection of cardiovascular risk factors and the effectiveness of therapy to achieve and sustain treatment goals. One of the main components of such interventions is the treatment of hypercholesterolemia, which is based on lifestyle modifications and lipid-lowering agents (i.e. statin therapy). This approach has been proved to be cost-effective.[1] While the greatest absolute risk reduction is achieved for cases at high risk for having a cardiovascular event,[2] due to current guidelines a large proportion of the users of lipid-lowering therapies are individuals with an intermediate CHD risk. As a result, the target population for CHD prevention programs has rapidly expanded in aging societies such as Mexico. In addition, due to the efficacy and safety of statin therapy, the achievement of lipid goals is one of the most feasible treatment targets in a CHD prevention program; nevertheless, barriers exist that are primarily related to cost and adherence issues. Thus, to achieve the desired effectiveness it is desirable to use lipid lowering therapies for properly selected patients based on strategies designed to overcome obstacles. To reach this objective, the first step is to assess the size of the population that qualifies for lipid lowering interventions and to characterize the target groups.

The National Health and Nutrition Survey 2006 (ENSANUT 2006) is a survey conducted by the Ministry of Health of Mexico designed to estimate the prevalence of obesity, type 2 diabetes, renal pathology, hypertension and dyslipidemia, among many other health conditions. Using this population-based, nationwide data, we describe the number and the characteristics of Mexican adults who are eligible for treatment using current guidelines [i.e. 2004 National Cholesterol Education Program (NCEP) recommendations].[3]

Material and Methods

Population sample

The objectives and design of the survey are described in detail in another report in this issue. In summary, this is a cross-sectional study that has representativeness for individuals living in metropolitan areas (state capitals or cities with a population above 100 000 people) and urban (population 2 500 to 99 999 inhabitants) and rural (less than 2 500 inhabitants) settings. A multistage, stratified and probabilistic sampling procedure was used. The country was divided into four regions (northeast, northwest, central and southern). All states in Mexico were included. A random sample of Basic Geographical Statistical Units was obtained in each state and neighborhood blocks were randomly selected. From every home, one randomly selected adult, adolescent and infant, and one health service user were invited to participate. Military, religious, health and other institutions were excluded. A target of 4 731 individuals and 1 476 households per state was estimated. The sample size was considered capable of detecting risk factors at the state level, with a prevalence of at least 8.1%, a relative error of estimation of 0.25, a design effect of 1.7 and a non-response rate of 20%. The number of households was increased to 1 620 in 13 states to assure enough power to be representative of the communities participating in the *Oportunidades* program. The total number of households was 48 600. This sample size allows the assessment of conditions with a prevalence equal to or greater than 0.4%. The study was conducted in accordance with the Helsinki Declaration of Human Studies and informed consent was obtained from each participant. A separate consent form was signed by participants who provided blood samples. The research and ethics committees of the Instituto Nacional de Salud Pública approved the study protocol.

Personal interview

A general structured interview was conducted. A previously standardized questionnaire was used to obtain information on demographic and socioeconomic aspects, family health history, personal medical history, and lifestyle factors such as smoking. It includes questions about pre-diagnosed hypercholesterolemia and hypertriglyceridemia and the current use of hypolipidemic agents. Anthropometric and blood pressure measurements were obtained during the same visit. 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-minute rest. 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

Blood samples were obtained from approximately 30% of the adult population. A random sub-sample of subjects with 8 or more hours of fasting was obtained (n=6 613). This report includes the results of 4 040 subjects who had the 9- to 12- h fasting period required for a complete lipid profile. The subjects were sampled at their homes and remained seated for 5 minutes before the blood was drawn.

All analytical measurements were done at the Instituto Nacional de Salud Pública. The sampling procedure was standardized during a two-week training course.

Total cholesterol was determined using enzymatic hydrolysis and oxidation. Triglycerides concentration was measured after lipase hydrolysis in an automatic analyzer with a tungsten lamp (Prestige 24i, Tokyo Boeki Medical System LTD, Tokyo, Japan). The interassay CV was 3.04% for total cholesterol and 5.7% for triglycerides. HDL-cholesterol was measured by an enzymatic colorimetric direct method after eliminating chylomicrons, VLDL, and LDL by enzymatic digestion; the interassay CV was 5.02%. To assure the precision of the determinations, the concentrations of total cholesterol, HDL-cholesterol and triglycerides were adjusted to a standard curve constructed with the determinations of NIST materials 909b and 1951b, levels I and II, using the standard material and a 1:1 dilution.

Definitions

NCEP-III guidelines were applied to each subject. The NCEP-III strategy stratifies the intensity of the lipid lowering therapy based on the absolute risk of having CHD. In this report, drug therapy was considered as required using the conservative approach of the NCEP-III report, since the majority of the hypercholesterolemia cases are not treated by specialists. The selection criteria for treatment are shown in Table I. A CHD equivalent was defined by the existence of a self-reported myocardial infarction or stroke, a non-traumatic amputation or diabetes. Positive risk factors for CHD include age (≥45 years for men or ≥ 55 for women), family history of CHD, current cigarette smoking, hypertension (blood pressure ≥ 140/90 mm Hg or use of antihypertensive medication) and low HDL-cholesterol (< 40 mg/dl). An HDL-cholesterol ≥ 60 mg/dl is considered a negative risk factor, allowing for the removal of one point from the sum of risk factors. Regrettably, the family history of coronary heart disease was not included in the questionnaire. For cases with two or more risk factors and free of a condition considered as a CHD equivalent, the 10-year absolute risk of having CHD was calculated with sex- and age-specific Framingham score sheets. The number of cases requiring lifestyle changes or drug therapy was calculated accordingly.

Diabetes was considered present if it was previously diagnosed by a physician or a fasting blood glucose value ≥ 7 mmol/L (126 mg/dL) was found in a subject without 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. Smoking was defined as any tobacco consumption during the month previous to sampling. Metabolic syndrome was diagnosed using NCEP criteria.[4]

Statistical analysis

The database was validated through recognition of missing values, outliers and inconsistencies between variables. Due to the characteristics of the survey design, the sample was analyzed as a complex one using SPSS for Windows, version 15. Weights were assigned to correct potential deviations from the age and sex distribution reported in the 2000 population census. Data are presented as medians and 95% confidence intervals (95%CI). Cases with triglycerides above 400 mg/dl were not considered for the estimation of the corresponding values for LDL cholesterol.

Table I
National Cholesterol Education Program-III treatment recommendations. Mexico, ENSANUT 2006

Risk category	*LDL-C goal*	*LDL-C threshold for lifestyle modifications*	*LDL-C threshold for drug therapy*
Coronary heart disease (CHD) or an equivalent condition (diabetes, stroke, arterial insufficiency of the lower limbs)	< 100 mg/dl	< 100 mg/dl	< 100 mg/dl
≥ 2 cardiovascular risk factors* and a 10-year risk of CHD > 20%	< 100 mg/dl	≥ 100 mg/dl	≥ 100 mg/dl
≥ 2 cardiovascular risk factors* and a 10-year risk of CHD 10-20%	< 130 mg/dl	≥ 130 mg/dl	≥ 130 mg/dl
≥ 2 cardiovascular risk factors* and a 10-year risk of CHD < 10%	< 130 mg/dl	≥ 130 mg/dl	≥ 160 mg/dl
< 2 cardiovascular risk factors*	< 160 mg/dl	≥ 160 mg/dl	≥ 190 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/dl). High HDL cholesterol (≥60mg/dl) is a negative risk factor and a positive risk factor is removed from the total count by its presence

Results

In this analysis, 4 040 cases were studied (1 871 men and 2 169 women). Their median age was 40.3 years (95%CI 39.5-40.9). Median lipid concentrations were: cholesterol 198.5 mg/dl, triglycerides 139.6 mg/dl, HDL-cholesterol 39.0 mg/dl, non HDL-cholesterol 159.5 mg/dl and LDL-cholesterol 131.5 mg/dl. The prevalence of lipid disorders is described in detail in another paper included in this issue of *Salud Pública de México.* Hypercholesterolemia was medically diagnosed prior to the survey for 8.6% (7.2-10.1%) of participants, and lipid lowering drugs were used by 4.6% (3.1-6.7%). However, the questionnaire was not accurate enough to assure that patients were taking their medications during the few days previous to their evaluation.

A CHD equivalent was found in 13.8% of the subjects. Two or more risk factors in the absence of a CHD equivalent were found in 31.5% of the population. The remaining 54.7% had one or less cardiovascular risk factor and 17.3% did not have any of these conditions. Thus, independent of the LDL-C concentration, almost half of the Mexican adults are potential candidates for lipid lowering therapy due to their medium to high risk of having CHD.

The distribution of the LDL-C concentrations, stratified by the thresholds proposed by the NCEP-III report, is shown in Table II. While 25% of study subjects had an optimal LDL-C (<100 mg/dl), for 11.2% of the population the LDL-C concentration was high enough to be a potential indication for a lipid-lowering drug therapy (> 190 mg/dl), independent of other risk factors. Thus, the majority of cases that qualify for drug treatment do so because they have moderate hypercholesterolemia and coexisting co-morbidities that increase their cardiovascular risk.

Table III shows the estimated number of Mexicans in each risk category and the distribution of their LDL-C concentrations. The sample analyzed in this report is representative of 33 775 193 adults. A CHD equivalent may be present in more than 4 million Mexicans. In addition, two or more risk factors may exist in nearly 10 million adults. If the Framingham tables are applied, the majority of those (74%) had an absolute risk of having CHD lower than 10%. It is estimated that there are more than 7 million Mexican adults who have a 10-year risk of having CHD of greater than 10% .

The percentage of cases that qualified for treatment according to the NCEP-III report is shown in Table IV, as

Table II

PERCENTAGE OF SUBJECTS WITH INCREASED LOW DENSITY LIPOPROTEIN CHOLESTEROL (LDL-C) CONCENTRATIONS, STRATIFIED ACCORDING TO THE PRESENCE OF CORONARY HEART DISEASE OR CARDIOVASCULAR RISK FACTORS (N=4 040). MEXICO, ENSANUT 2006

	LDL- C (mg/dl)					
Strata [n (% between group)]	*<70*	*70-99.9*	*100-129.9*	*130-159.9*	*160-189.9*	*≥ 190*
Coronary heart disease or diabetes	10.1	19.4	21.4	22.5	15.3	11.3
[n= 557 (13.8 %)]	(7.4-13.6)	(14.9-24.7)	(16.3-27.6)	(16.4-30)	(11.3-20.3)	(8.2-15.4)
CHD, stroke or arterial insufficiency in lower	4.7	26.9	40.1	6.2	15.4	6.7
limbs (n=51)	(1.6-13)	(12.5-48.6)	(21.6-61.8)	(2.2-15.9)	(6.6-32.1)	(2.4-17.6)
Diabetes (n=506)	10.5	18.1	21.3	23.7	14.9	11.5
	(7.6-14.2)	(13.7-23.6)	(16.0-27.8)	(17.3-31.5)	(10.8-20.2)	(8.3-15.7)
Without CHD or diabetes						
Two or more risk factors	8.2	23.1	30.8	19.4	10.6	7.9
[n=1272 (31.5%)]	(6.1-10.8)	(19.6-27.0)	(26.9-35.0)	(16.4-22.8)	(8.4-13.4)	(6.0-10.3)
10-year risk	3.8	15.8	12.9	10.1	27.2	30.3
> 20 [n=89 (2.2%)]	(0.9-14.6)	(7.4-30.6)	(7.1-22.2)	(5.0-19.2)	(13.9-46.3)	(17.0-48.0)
10-year risk	4.0	18.4	22.2	21.3	18.8	15.2
10-20% [n=241 (5.9%)]	(2.2-7.2)	(11.9-27.4)	(15.3-30.9)	(15.5-23.7)	(13.1-26.3)	(10.1-22.3)
10-year risk	9.6	24.9	34.7	19.8	7.0	3.9
< 10% [n=942 (23.3%)]	(7.0-13.0)	(20.8-29.6)	(29.7-40.1)	(16.2-24.0)	(5.0-9.7)	(2.5-6.1)
< 2 risk factor	6.3	15.6	29.2	22.6	13.6	12.7
[n= 2211 (54.7%)]	(4.9-8.1)	(13.3-18.3)	(26.4-32.2)	(19.9-25,4)	(11.4-16.1)	(10.7-15.0)
Total	7.3	18.4	28.6	21.4	13.1	11.2
(n=4040)	(6.2-8.6)	(16.6-20.3)	(26.6-30.8)	(19.4-23.5)	(11.5-14-8)	(9.8-12.8)

Table III

Estimated number of Mexicans in each cardiovascular risk category and their low density lipoprotein cholesterol (LDL-C) concentrations (mg/dl). Mexico, ENSANUT 2006

Strata [n (% between group)]	*LDL- C (mg/dl)*					
	<70	*70-99.9*	*100-129.9*	*130-159.9*	*160-189.9*	*≥ 190*
Coronary heart disease or diabetes	473 121	905 843	1 003 612	1 052 156	715 550	530 815
Total: 4 681 099	(313 255-	(649 846-	(732 558-	(652 844-	(500 948-	(357 924-
(4 031 350-5 330 848)	632 987)	1 161 841)	1 274 665)	1 451 467)	930 151)	703 706)
CHD, stroke or arterial insufficiency in lower limbs	21 414	122 524	182 484	28 123	70 342	30 695
Total: 455 585	(0- 43 273)	(25 011-	(44 694-	(840-55 407)	(10 545-	(305-61 085)
(272 562-638 609)		220 038)	320 273)		130 139)	
Diabetes	459 774	793 329	933 776	1 036 489	654 642	504 299
Total: 4 382 311	(300 839-	(554 530-	(668 230-	(637 531-	(446 223-	(339 235-
(3 744 465-5 020 157)	618 708)	1 032 128)	1 199 322)	1 435 447)	863 061)	669 363)
Without CHD or diabetes						
Two or more risk factors	814 493	2 302 731	3 075 076	1 939 470	1 062 327	786 587
Total: 9 980 686	(574 865-	(1 894 750-	(2 553 217-	(1 607 155-	(795 378-	(569 478-
(9 149 490-10 811 883)	1 054 120)	2 710 711)	3 596 936)	2 271 786)	1 329 275)	1 003 697)
10 year risk > 20	26 548	110 386	90 125	70 563	190 032	211 690
Total:698 648	(6 287-	(51 699-	(49 604-	(34 932-	(97 112-	(118 770-
(640 464-756 831)	102 002)	213 786)	155 099)	134 140)	323 474)	335 351)
10-year risk 10-20%	74 655	343 415	414 338	397 540	350 881	283 691
Total:1 866 388	(41 060-	(222 100-	(285 557-	(102 651-	(244 496-	(188 505-
(1 710 955-2 021 822)	134 380)	511 390)	576 714)	442 334)	490 860)	416 204)
10-year risk < 10%	709 028	1 794 727	2 562 841	1 462 370	516 999	288 042
Total: 7 385 708	(516 999-	(1 536 227-	(2 193 555-	(1 196 485-	(369 285-	(184 642-
(6 770 623-8 000 794)	960 142)	2 186 170)	2 961 669)	1 772 570)	716 413)	450 528)
< 2 risk factor	1 136 781	2 821 080	5 261 698	4 065 893	2 447 483	2 293 144
Total: 18 026 081	(847 224-	(2 322 366-	(4 645 146-	(3 531 145-	(2 014 806-	(1 886 621-
(16 994 868-19 057 295)	1 426 339)	3 319 794)	5 878 249)	4 600 641)	2 880 159)	2 699 668)
Total	2 457 006	6 199 923	9 670 950	7 232 825	4 426 683	3 787 805
n= 33 775 193	(2 036 223-	(5 532 885-	(8 836 311-	(6 465 504-	(3 831 702-	(3 240 296-
(32 238 121-35 312 265)	2 877 788)	6 866 960)	10 505 588)	8 000 145)	5 021 664)	4 335 315)

is the expected number of individuals that may qualify for lifestyle modification and drug therapy. Almost 30% of the population was found to be eligible for a lipid-lowering therapy, lifestyle modifications were required for 36.25% of the cases and the addition of drug therapy was required for 24.19% of Mexican adults. Thus, nearly 12 million Mexicans should be educated to change their lifestlyles. Also, close to 8 million individuals require drug therapy to decrease their cardiovascular risk.

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 (70.5% for both lifestyle modification and drug therapy). Almost 75% of the patients with diabetes require statin therapy due to their LDL-C. The stratification of the population with two or more cardiovascular risk factors, using the NCEP-III approach, shows notable differences in the percentages of cases that qualify for therapy. For example, 80% of individuals with a 10-year risk greater than 20% qualify for drug therapy. In contrast, only 10.9% of the subjects with a 10-year risk less than 10% may need drug therapy. This percentage is not different than that found for low-risk cases (i.e. cases with less than two risk factors).

A separate analysis was performed of non-diabetic cases with metabolic syndrome (n=1 224). Less than two NCEP-III risk factors were present in 564 cases (46.1%), of which only 14.3% had an LDL-C > 190 mg/dl (the LDL-C threshold for receiving any form of lipid-lowering treatment). Two or more risk factors were present for

Table IV
DISTRIBUTION OF TREATMENT FOR ELIGIBLE PATIENTS. MEXICO, ENSANUT 2006

Strata [n (% between group)]	*Lifestyle modification*	*Population*	*Drug therapy*	*Population*
Coronary heart disease or diabetes	70.5	3 302 133	70.5	3 302 133
	(65.8-75.8)	(2 857 776-3 919 936)	(65.8-75.8)	(2 857 776-3 919 936)
CHD, stroke or arterial insufficiency in lower limbs	74.4	311 644	74.4	311 644
	(47.5-83.4)	(154 536-468 757)	(47.5-83.8)	(154 536-468 757)
Diabetes	71.4	3 129 206	71.4	3 129 206
	(66.6-76.8)	(2 692 681- 3 739 178)	(66.6-76.8)	(2 692 681-3 739 178)
Without CHD or diabetes				
Two or more risk factors	38.6	3 861 933	23.9	2 399 563
	(31.2-49.3)	(2 861 507-4 920 600)	(18 4-29.4)	(906 290-2 987 394)
10-year risk > 20	80.5	562 410	80.5	562 410
	(43-100)	(300 710-698 684)	(43-100)	(300 710-698 684)
10-year risk 10-20%	55.3	1 032 112	55.3	1 032 112
	(43,4-68,7)	(810 385-1 282 405)	(38.7-71.9)	(810 385-1 282 405)
10-year risk < 10%	30.7	2 267 411	10.9	805 041
	(23,7-39.8)	(1 750 412-2 939 511)	(7.5-15.1)	(605 580-1 006 305)
< 2 risk factor	26.3	4 740 627	12.7	2 293 144
	(23.7-29.4)	(3 901 427-5 579 847)	(10.7-15.0)	(1 883 136-2 780 537)
Total	36.25	11 904 693	24.19	7 994 840
	(28,4-42.7)	(9 620710-14 420 383)	(16 7-28.7)	(5 647 202-9 687 867)

the remaining 660 cases (53.9%). For the majority of this subgroup (75%), the estimated 10-year risk was less than 10%; as a result, the LDL-C threshold for drug therapy is greater (≥160 mg/dl) for this group. Thus, only 12.4% of subjects with a 10-year risk qualify for drug therapy, and pharmacologic treatment is applicable to 54.2% of subjects with a 10-year risk of 10-20% and 80.6% of those with a 10-year risk greater than 20%. However, only a minority of metabolic syndrome cases falls within these categories (18.6 and 6%, respectively, of those with two or more cardiovascular risk factors). Thus, NCEP guidelines make it unlikely for non-diabetic patients with metabolic syndrome to receive statin therapy; only 15.7% qualify for drug therapy.

Because of the high prevalence of hypertriglyceridemia in our population, we assessed the effects of using the non HDL-cholesterol instead of the LDL-C as the prime goal of therapy.[16-18] The results are shown in Table V. The distribution of the non-HDL-cholesterol strata was very similar to that found for the LDL-C. As a result, the number of cases that qualifies for receiving treatment was not modified; this was true for all three cardiovascular risk categories. For example, among the patients with diabetes, (the group for which the LDL-C is most likely to be underestimated), the number of cases that have the recommended LDL-C or non-HDL-cholesterol was nearly the same (71.4% for LDL-C<100 mg/dl and 72.7% for non-HDL-cholesterol<130 mg/dl).

Discussion

The NCEP-III guideline is the standard of care for dyslipidemic cases in many countries. It recommends the identification of high-risk medical conditions, the collection of major risk factors and the calculation of the 10-year risk, using Framingham score sheets when appropriate. LDL-C goals are stratified based on the absolute CHD risk. Also, several groups have used it as a tool for epidemiological studies in order to describe the overall cardiovascular risk of a population.[5] This report describes the prevalences of CHD risk groups (as defined by the NCEP-III document) and the achievement of LDL-C treatment targets in the ENSANUT 2006 survey (a population based, nationwide study representative of urban Mexican adults aged 20 or older). In Mexico, a coronary heart disease equivalent was found in 13.8% of the population studied and two or more risk factors were detected in an additional 31.5%. Nearly 30% of the study population qualified for some form of lipid-lowering therapy; LDL-C lowering drug treatment was

Table V

Percentage of subjects with increased non-high density lipoprotein cholesterol (non-HDL-C) concentrations, stratified according to the presence of coronary heart disease or cardiovascular risk factors (n=4 040). Mexico, ENSANUT 2006

Strata (n [% between group])	*Non-HDL- C (mg/dl)*				
	<100	*100-129.9*	*130-159.9*	*160-189.9*	*≥ 190*
Coronary heart disease or diabetes	10.5	17.8	21.5	24.9	25.3
(n= 557 [13.8 %])	(7.7-14.1)	(13.5-23.1)	(16.3-27.9)	(18.7-32.4)	(20.5-30.8)
CHD, stroke or arterial insufficiency in lower limbs (n=51)	13.8	20.3	14.9	28.3	22.8
	(4.7-34.2)	(9.0-39.7)	(6.6-30.2)	(11.6-40.0)	(11.5-40.0)
Diabetes(n=506)	9.8	17.5	21.9	26.0	24.8
	(7.2-13.3)	(13.1-22.9)	(16.3-28.6)	(19.5-33.8)	(19.8-30.6)
Without CHD or diabetes					
Two or more risk factors (n=1 272 [31.5%])	9.9	24.4	30.8	17.0	17.9
	(7.8-12.4)	(21.0-28.1)	(26.7-35.2)	(14.4-20.1)	(15.1-21.1)
10-year risk > 20 (n=89 [2.2%])	4.7	16.7	10.1	11.2	57.3
	(1.4-14.8)	(8.0-31.5)	(5.3-18.4)	(5.8-20.7)	(41.6-71.7)
10-year risk 10-20% (n=241 [5.9%])	5.0	17.6	24.6	19.5	33.3
	(3.0-8.5)	(11.3-26.4)	(17.4-33.5)	(14.1-26.3)	(25.4-42.3)
10-year risk < 10% (n=942 [23.3%])	11.4	26.7	34.4	17.2	10.3
	(8.7-14.8)	(22.6-31.3)	(29.2-40.0)	(13.9-21.1)	(7.9-13.2)
< 2 risk factor (n= 2 211 [54.7%])	8.2	18.7	28.5	19.9	24.8
	(6.4-10.4)	(16.5-21.0)	(25.7-31.6)	(17.4-22.6)	(22.3-27.5)
Total (n=4 040)	9.0	20.3	28.3	19.7	22.7
	(7.7-10.6)	(18.6-22.1)	(26.0-30.6)	(17.8-21.8)	(20.8-24.7)

recommended for 24.19%. Our data helps to estimate the magnitude of the burden imposed on the Mexican health system by lowering LDL-C for cardiovascular prevention. Applying our results to the segment of the population covered by this survey, more than 7.9 million cases nationwide may require LDL-lowering drug therapy, according to NCEP-III criteria.

The NCEP-III approach directs intervention to the cases with the highest risk. This report shows that 13.8% of the population represented by ENSANUT 2006 (i.e. 4.6 million adults) meets the definition of a CHD equivalent, and patients with diabetes compose the majority of this group. However, we recognized that other conditions considered as CHD equivalents (i.e. myocardial infarction and others) are under-represented because their prevalences are not high enough to be precisely measured given the number of cases studied here. Among the high-risk group, the majority of cases have LDL-C above the treatment target, and only 29.5% of those have LDL-C <100 mg/dl. The goal of intensive lipid-lowering therapy (LDL< 70 mg/dl) is achieved only for 10.1% of cases. Lipid-lowering treatment (statin therapy and lifestyle modifications) will be needed for 70.5% to reach the LDL-C goal, and it is likely that high-dose statin therapy will be required for 26.6% of this group (i.e. cases with LDL-C >160 mg/dl), since reaching the treatment goal using the standard statin dose is not likely.[6] Additionally, cases with two or more risk factors and a 10-year risk greater than 20% are considered part of the high-risk group, which modestly increases the size of this group. Though only 2.2% of the population (0.69 million cases) is included in this high-risk subgroup, these cases are characterized as being the cluster with the highest LDL-C levels among the high-risk individuals, with 57.5% having LDL-C>160 mg/dl. Our data show that effective CHD prevention based on the modification of plasma lipid levels is far from being achieved, even for the high-risk group, which should be the prime target for prevention programs because it represents the population for which lipid-lowering therapy has the highest cost-effectiveness ratio.

The next group to be considered is composed of cases with two or more cardiovascular risk factors and a 10-year risk of less than 20%. In contrast to the recom-

mendations for the high-risk group, the NCEP-III actions for the intermediate- and low-risk individuals are based mainly on consensus statements by expert groups[7] because the evidence for these populations is insufficient or biased by the inclusion criteria used by existing studies.[8] Thus, these recommendations are controversial, but highly relevant since they are applicable to almost 30% of the population. And while the use of the Framingham tables, as proposed by the NCEP-III report, attempts to better identify the high-risk cases among subjects with two or more risk factors, concerns have been expressed about its use in non-Caucasian populations because the score overestimates the risk for these ethnic groups.[9] Also, the Framingham tables have an unsatisfactory predictive power for metabolic syndrome and other conditions associated with CHD (i.e. primary hyperlipidemias, organ transplant recipients).[10] In our survey, the majority (74%) of the group with ≥ 2 risk factors was identified as having a 10 year-risk of CHD less than 10%. As a consequence, the use of the Framingham risk score and the NCEP-III approach makes it improbable that the majority of these subjects will qualify for drug therapy. Although this fact is highly desirable from the economic point of view,[11] it may leave a large number of at-risk individuals untreated due to the presence of conditions not included in the Framingham risk score. When we assessed the NCEP-III strategy in non-diabetic cases with metabolic syndrome, a common condition among Mexican adults, we found that less than two NCEP-III risk factors were present in nearly half of this population (46.1%). Additionally, the majority of the cases with two or more risk factors (75%) had a 10-year risk less than 10%. As a consequence, only 15.7% of the non-diabetic cases with metabolic syndrome qualified for pharmacologic treatment; this percentage is only slightly greater than that observed for the low-risk group and contrasts with the well-described risk for coronary events in metabolic syndrome [2.7 (95CI% 1.2-6.2%)];[12] in absolute terms, metabolic syndrome represents a 10-year cardiovascular risk of 10-20%.[13] These data clearly reflect just how variable the number of cases requiring drug therapy could be in the intermediate risk group. Because CHD predictive scales are heavily influenced by ethnicity and environmental factors and the required information could not be obtained from the literature,[14] longitudinal studies in Mexican adults are needed to design cost-effective strategies applicable to our population.

The last group to be analyzed is that of low-risk individuals (i.e. those with one risk factor or less). As expected, they are the group in which diet and drug therapy are required less often. However, a surprising finding is the high percentage (12.7%) of this group that has LDL-C above 190 mg/dl, which is several times higher than the percentage found (0.5%) in a previous Mexican population-based survey.[15] It is even greater than the percentage reported in the US (2.4%).[16] Additional studies will be needed to identify the potential explanations for this result.

Strengths and limitations must be recognized. The ENSANUT 2006 survey updates the information provided by two previous, large population-based surveys conducted in 1994[15] and 2000.[17] We recognize as limitations of this report that cardiovascular disease was diagnosed by self-report; this approach may result in underestimation of the prevalence. Also, family history of coronary heart disease was not registered. In addition, there is no information about other relevant variables for the estimation of cardiovascular risk (e.g. physical activity and mental stress).

Conclusion

In summary, prevention of cardiovascular disease based on the modification of LDL-C levels represents an enormous challenge for the Mexican society. Of the 33.7 million adults represented in the ENSANUT 2006 survey, 36.25% requires the adoption of a healthy lifestyle and 24.19% qualifies for drug therapy. In other words, nearly 11.9 million adults should be treated regularly by a physician and a dietitian to change their dietary habits and to increase their physical activity. Also, close to 7.9 million will require statin therapy for a long period of time, which represents a heavy economic burden on the health system. Despite the large number of patients that require therapy, few are diagnosed and treated properly. This remarkable effort should be implemented for several reasons. First, CHD is the most common cause of death in Mexican adults.[18] Second, lipid disorders are highly prevalent in our population.[19] Third, 45.3% of the population represented by ENSANUT 2006 is at a high- (13.8%) or intermediate- (31.5%) risk for having CHD. And, fourth, solid evidence exists to support lipid-lowering treatments as a cost-effective therapy to reduce the incidence of CHD events.[1] Multiple changes in our health system are urgently needed to achieve this goal. Medical school curricula should be updated so that students become competent in the treatment of lipid disorders. In addition, primary care physicians and specialists should be trained to provide effective prevention. Finally, the health system should design strategies to achieve the required adherence to therapy.[20]

Conflicts of interest

We declare that we have no conflicts of interest.

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