

SERUM TOTAL, FRACTIONATED CHOLESTEROL CONCENTRATION DISTRIBUTION AND PREVALENCE OF HYPERCHOLESTEROLEMIA IN SAUDI ARABIA, REGIONAL VARIATION

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This is a study of the regional variation in Saudi Arabia with respect to the pattern of distribution of total serum cholesterol concentration, low-density lipoprotein (LDL), high-density lipoprotein (HDL), total cholesterol to HDL ratio (CH/HDL) and prevalence of hypercholesterolemia (HC) among Saudi population. It is a cross-sectional national epidemiological randomized household survey. The subjects consisted of 4548 Saudis over the age of 15 years. The sample was representative and in accordance with the national population distribution with respect to age, gender, regional and residency population distribution. Blood samples were drawn and assayed for total cholesterol concentration (TCC), triglyceride and high-density lipoprotein concentration. Low-density lipoprotein and total cholesterol/high-density lipoprotein ratio were calculated. The mean serum TCC of female subjects was higher than for male subjects across all regions; however, the difference reached a significance only in the Southern and Western regions. The 90th percentile of serum TCC for male subjects was either equal to or higher than that for female subjects at early age groups across all regions; however, the 90th percentile of serum TCC for female subjects was higher than for male subjects at older age groups across all regions. Mean serum HDL concentration for female subjects was either equal to or higher than for male subjects across all regions, except the Central region. The difference, however, reached a significance in the Western region only. The prevalence of borderline high HC (5.2 to 6.2 mmol/L) was higher among male subjects in the Central region and equal between male and female subjects of Western and Eastern regions and higher among female subjects in the Northern and Southern regions. The prevalence of high HC (>6.2 mmol/L) was higher among female subjects compared with male subjects across all regions. The highest and lowest prevalence of high HC among male subjects in the Eastern and Northern regions, respectively, while the highest and lowest prevalence of high HC among female subjects were in the Eastern and Northern regions. The prevalence of HC (>5.2 mmol/L) among subjects over the age of 40 years was highest and lowest for male subjects of Eastern and Southern regions, respectively, and for female subjects of Eastern and Western regions, respectively. There was a variable pattern of serum total and fractionated cholesterol concentration distribution among Saudi subjects. It appears, however, that at large, the subjects of the Eastern and Northern regions had the highest and lowest prevalences of cholesterol-related risk factors for CVD, respectively. There is a need to study the underlying factors for the regional variation with respect to cholesterol-related risk factors with emphasis on nutritional habits, including the quantity and quality of food, the prevalence of obesity, glucose intolerance and smoking. Identification of such factors is essential for monitoring the effectiveness of any future plan for combating cholesterol-related risk factors for CVD. *Ann Saudi Med 1997;17(2):179-184.*

Cardiovascular diseases (CVD) is the leading cause of death in developed countries.¹ There has been change in the incidence of CVD over the last 30 years, with increasing incidence in the developing countries.^{2,3} CVD events are the ultimate result of interaction of several risk factors, such as hypertension, smoking, obesity, diabetes

mellitus and hypercholesterolemia.⁴

Hypercholesterolemia (HC) is an important independent risk factor in the process of progression of atherosclerosis.^{5,6} Studies have shown regression of atheroma as shown by angiogram and decreased incidence of CVD events using hypocholesterolemic drugs.^{7,8}

The prevalence of HC (>5.2 mmol/L) in Saudi Arabia, through population-based epidemiological study for Saudi subjects over the age of 15 years was 16% and 19% for male and female subjects, respectively.⁹

CVD events are major causes of morbidity and mortality among the Saudi population.^{10,11}

Saudi Arabia is divided into five major administrative

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Accepted for publication 22 September 1996. Received 27 May 1996.

TABLE 1. Serum total cholesterol concentration (mmol/L) distribution for men in different regions of Saudi Arabia.

Region	Age group (year)	Number	Mean	SD	Percentile		
					10th	50th	90th
West	15-20	166	3.4	1.3	2.2	3.1	5.2
	21-30	177	3.8	1.3	2.3	3.5	5.4
	31-40	141	4.1	1.4	2.5	4.0	5.9
	41-50	77	4.4	1.5	2.7	4.1	6.4
	51-60	42	4.2	1.2	2.9	3.9	6.0
	>60	45	4.5	1.2	3.2	4.4	6.1
	All	648	3.9	1.4	—	—	—
Central	15-20	134	3.6	1.3	2.2	3.4	5.3
	21-30	196	4.2	1.7	2.5	3.9	6.6
	31-40	99	4.2	1.4	2.6	4.1	6.3
	41-50	75	4.3	1.4	2.6	4.2	6.1
	51-60	47	4.2	1.5	2.7	3.8	6.0
	>60	38	4.3	1.2	2.8	4.2	5.7
	All	589	4.1	1.5	—	—	—
South	15-20	131	3.5	1.2	2.2	3.4	4.7
	21-30	159	3.9	1.2	2.6	3.7	5.2
	31-40	101	4.3	1.3	2.7	4.3	5.8
	41-50	71	4.4	1.3	3.0	4.2	6.0
	51-60	42	4.5	1.9	3.0	4.3	5.5
	>60	36	4.3	1.0	2.8	4.3	5.7
	All	540	4.0	1.3	—	—	—
East	15-20	74	3.5	1.1	2.2	3.4	4.9
	21-30	111	4.1	1.3	2.5	4.0	6.0
	31-40	62	4.7	2.1	2.5	4.3	6.5
	41-50	40	4.7	2.2	3.1	4.1	5.8
	51-60	27	4.6	1.1	2.1	4.6	7.4
	>60	21	4.9	1.6	3.0	4.6	6.9
	All	335	4.2	1.7	—	—	—
North	15-20	40	3.5	1.4	2.3	3.7	4.4
	21-30	59	3.2	0.8	2.2	3.1	4.2
	31-40	35	4.0	1.0	2.7	4.0	5.3
	41-50	21	4.1	1.0	3.1	4.0	5.4
	51-60	16	4.6	1.6	3.1	4.0	5.6
	>60	11	4.2	1.3	2.6	4.0	5.9
	All	182	3.7	1.2	—	—	—

TABLE 2. Serum total cholesterol concentration (mmol/L) distribution for women in different regions of Saudi Arabia.

Region	Age group (year)	Number	Mean	SD	Percentile		
					10th	50th	90th
West	15-20	167	3.8	1.2	2.5	3.7	5.2
	21-30	181	4.3	1.7	2.6	4.0	6.1
	31-40	122	4.3	1.4	2.7	4.0	5.9
	41-50	90	4.2	1.2	3.0	4.0	5.9
	51-60	31	4.4	1.6	2.9	4.1	6.0
	>60	31	4.4	1.3	2.8	4.2	6.2
	All	622	4.2	1.4	—	—	—
Central	15-20	129	3.8	1.4	2.2	3.7	5.7
	21-30	188	4.6	2.1	2.8	4.1	6.9
	31-40	104	4.4	1.5	2.6	4.1	6.1
	41-50	67	4.3	1.4	2.6	4.0	6.4
	51-60	41	4.7	1.6	3.1	4.5	7.1
	>60	28	4.0	1.4	2.0	4.0	4.9
	All	557	4.3	1.7	—	—	—
South	15-20	125	3.9	1.1	2.7	3.8	5.3
	21-30	187	4.3	1.3	2.8	4.2	5.9
	31-40	95	4.4	1.1	3.0	4.5	5.7
	41-50	70	4.4	1.1	3.2	4.4	5.5
	51-60	47	4.6	1.1	3.3	4.4	6.3
	>60	36	4.8	1.3	3.3	4.8	5.9
	All	560	4.3	1.2	—	—	—
East	15-20	74	3.9	1.5	2.4	3.6	5.7
	21-30	115	4.2	1.6	2.2	4.1	6.2
	31-40	63	4.4	1.9	2.3	4.2	6.1
	41-50	39	5.1	1.6	3.1	4.8	7.4
	51-60	16	5.4	1.9	3.3	4.6	7.7
	>60	10	4.1	0.9	2.5	4.1	5.1
	All	317	4.3	1.7	—	—	—
North	15-20	41	3.3	0.9	2.2	3.2	4.2
	21-30	62	4.0	1.2	2.6	3.8	5.5
	31-40	35	3.8	1.2	2.3	3.9	5.4
	41-50	23	4.2	1.3	2.5	3.9	6.2
	51-60	15	4.4	1.4	2.4	4.2	6.0
	>60	13	4.0	1.2	1.9	3.9	5.6
	All	189	3.9	1.2	—	—	—

regions. There is a regional population variation with respect to demographic, social, economical, cultural and nutritional factors.

This is a study of regional variations with respect to serum total, fractionated cholesterol concentration distribution and prevalence of HC in Saudi Arabia.

Material and Method

Study Population

Saudi Arabia is a peninsula located in the Middle East. Most of the surface area, which exceeds 2,240,000 km², is desert. According to the National Population Census held in 1992, the Saudi population was 12 million, of which 70% are less than 30 years of age. About 60% and 40% of the population lives in urban and rural communities, respectively.

A National Epidemiological Household Survey for Chronic Metabolic Disorders, among them cholesterol-related diseases, was conducted among Saudi citizens over the age of 15 years in different regions of Saudi Arabia, between 1990 and 1993. As this was a national cholesterol study, which had several objectives, a large sample size of 20,000 subjects was calculated to fulfill all the objectives. The objective of this particular paper was to study serum total, fractionated cholesterol distribution, and prevalence of hypercholesterolemia among subjects of different regions of Saudi Arabia. A multistage stratified cluster random sampling technique was used for selection of the study population. The assigned population sample of the study was distributed between the different regions in accordance with the regional population distribution, as per the national population census (NPC). There was an initial adjustment for area type, urban versus rural, and

population distribution in each region as per the NPC. Cities and villages of each region were listed and then random selection was made of a certain number of cities and villages in accordance with the allocated share of each region in the national sample. The administrative maps of the selected cities and villages were reviewed and then there was a random selection of the number of districts in these cities and villages.

Primary care physicians who work in these localities were assembled and given orientation lectures and workshops in different aspects of the study, such as filling out the forms that include personal, demographic, social and medical history, such as a history of diabetes mellitus. Medical records of these patients were reviewed to confirm the diagnosis of diabetes mellitus. The primary care physicians were also trained in the proper method of handling blood and the measurement of height and weight, which was done at the Primary Care Clinic (PCC), usually two to three days after the initial visit to the homes.

Every third parallel street in any of these localities was selected and then every third house was included in this study. All Saudi citizens over the age of 15 years in these houses were asked to participate in this study. The response rate was 92%.

All the interviewed subjects were requested to attend the PCC for weight, height and blood measurements; however, only 69% showed up to the suggested appointments. Blood samples were drawn at random in an EDTA tube, centrifuged and the serum was frozen and stored until completion of the target sample of 100 and 50 subjects per physician in each district in city or village, respectively. The samples were sent frozen to the central laboratory at King Saud University, Riyadh, from all over the country. Samples were stored at -20°C until assayed. Upon completion, the target sample records were sent to the central office in Riyadh for data entry. A computer program was designed, using D-base IV software package for data entry. After completion of the data entry, there was a final adjustment for gender, age, regional, urban versus rural population distribution, in accordance with the NPC through random selection, using Statpack Gold software package, of a number of records from different regions and age groups. The final adjusted sample was 4548 subjects, 2294 (50%) were male and 2254 (50%) were female subjects.

Serum Lipid Analysis

Analysis was done using the Cobas Mira S Clinical Analyzer, Roche Diagnostics. Unimate-7-cholesterol and unimate-7-triglycerides were used for measuring total cholesterol and triglycerides, respectively.

The assay for total cholesterol was done using the enzymatic method, which is an enzymatic colorimetric test with cholesterol esterase and cholesterol oxidase.

Triglycerides were also assayed using an enzymatic colorimetric test with glycerol phosphate oxidase. Phosphotungstic acid and magnesium chloride, and a high-density lipoprotein (HDL) cholesterol-precipitating reagent were used to remove low-density lipoprotein (LDL) cholesterol, total cholesterol and very low density lipoprotein (VLDL), respectively, after which HDL cholesterol was determined by an enzymatic colorimetric method. LDL cholesterol was estimated by the formula $\text{LDL cholesterol} = \text{total cholesterol} - (\text{HDL cholesterol} + 0.46 \times \text{triglyceride})$. Fifty-four subjects with serum triglyceride concentration >4.5 mmol/L were excluded from LDL cholesterol calculation. The intra- and interassay coefficients of variation were 2.2% and 2.6%, respectively, for total cholesterol and 2.2% and 2.2%, respectively, for triglyceride.

Quality Control

Assay performance was monitored using the lipid control serum, control serum N (normal range) or control serum P (pathologic range) wherever applicable (Roche Diagnostics, Basel, Switzerland).

Total and Fractionated Cholesterol Concentration Definition

Hypercholesterolemia was defined as borderline high for cholesterol values between 5.2 and 6.2 mmol/L and high for cholesterol values >6.2 mmol/L. Hypo HDL cholesterolemia was defined for values lower than 0.9 mmol/L and considered a major risk factor for CVD, while HDL levels greater than 1.6 mmol/L can be considered a negative risk factor CVD. Total cholesterol/HDL cholesterol ratio values between 5.0 and 6.5 characterized individuals at intermediate risk, while ratio values higher than 6.5 characterized individuals at high risk of developing CVD.^{12,13}

Statistical Analysis

Statistical analysis was done using Statpack Gold (statistical analysis package). Data are presented as median, mean (SD), percentile, and percentage. Student's *t*-test was used for comparison between means and number of continuous variables, a *P*-value 0.05 was considered significant.

Results

There were 2294 (50%) male and 2254 (50%) female subjects, which constitutes the total sample for the national cholesterol study. The mean (SD) of age for male and female subjects were 33.1 (15.1) and 32.9 (14.9) years, respectively ($P=0.57$). There was no significant difference with respect to age among male and female subjects of any given region.

Serum Total and Fractionated Cholesterol Concentration Distribution

Mean serum TCC for female subjects was higher than for male subjects across all regions; however, the difference reached significance in the Southern and Western regions.

There was a progressive increase in mean serum TCC with age across most of the regions, with the highest achieved at the seventh decade for male subjects and a decade earlier for female subjects (Tables 1 and 2).

The 90th percentile of serum TCC for female subjects across all regions was higher than for male subjects for most of the age groups. The highest 90th percentile of serum TCC across most of the age groups was in the Eastern region for male and female subjects.

Mean serum LDL concentration for female subjects was higher than for male subjects across all regions except the Central region. Mean LDL concentration for female subjects was significantly higher than for male subjects in the Southern region only (Table 1).

There was a gender variation with respect to serum LDL concentration distribution among male and female subjects of any given region. The prevalence of hyper LDL cholesterolemia (>4 mmol/L) was higher among male subjects of Western and Northern regions, while it was higher among female subjects of Southern, Central and Eastern regions. The highest and lowest prevalence of hyper LDL cholesterolemia among male subjects was in the Western and Northern regions, respectively, while the highest and lowest prevalence of hyper LDL cholesterolemia among female subjects was in the Southern and Northern regions, respectively.

There was a significantly higher proportion of male subjects in the Northern region and female subjects in the Southern region with serum LDL concentration >4 mmol/L when compared with their counterpart subjects of the same region.

Mean serum HDL concentration for female subjects was either equal to or higher than that for male subjects across all regions except the Central region. The difference, however, reached a significance in the Western region only.

The prevalence of hypo HDL cholesterolemia (<0.9 mmol/L) was higher among male subjects of the Western, Central and Eastern regions, while it was higher among female subjects of the Northern region and equal between male and female subjects of the Southern region. The highest and lowest prevalence of hypo HDL cholesterolemia among male subjects was in the Western and Northern regions, respectively, while the highest and lowest prevalence of hypo HDL cholesterolemia among female subjects was in the Southern and Northern regions, respectively.

The prevalence of hyper HDL cholesterolemia (>1.6 mmol/L) was higher among male subjects of the Northern and Southern regions, compared with female subjects, while it was higher among female subjects of the Western and Eastern regions. The highest and lowest prevalence of hyper HDL cholesterolemia among male subjects was in the Northern and Western regions, respectively, while the highest and lowest prevalence of hyper HDL cholesterolemia among female subjects was in the Central and Southern regions, respectively.

There was a significantly higher proportion of male subjects in the Western and Eastern regions with serum HDL concentration <0.9 mmol/L, when compared with female subjects of the same regions.

The prevalence of high total cholesterol to HDL (CH/HDL) ratio (>6.5) was higher among males of Western, Northern, and Central regions compared with female subjects, while it was higher among female subjects of the Southern and Eastern regions. The highest and lowest prevalence of high CH/HDL ratio among male subjects was in the Western and Northern regions, respectively, while the highest and lowest prevalence of high CH/HDL ratio among female subjects was in the Southern and Northern regions, respectively.

The difference between male and female subjects of each region with respect to serum HDL >1.6 mmol/L, borderline high CH/HDL ratio (5-6.5) or high CH/HDL ratio (>6.5) does not reach a significance.

Prevalence of Hypercholesterolemia (HC)

There was a gender variation with respect to the prevalence of borderline high HC (5.2 to 6.2 mmol/L) or high (HC >6.2 mmol/L) among male and female subjects of any given region (Tables 3 and 4). The prevalence of borderline high HC was higher among male subjects in the Central region and equal between male and female subjects of Western and Eastern regions and higher among female subjects in the Northern and Southern regions.

The highest and lowest prevalence of borderline high HC among male subjects was in the Central and Northern regions, respectively, while the highest and lowest prevalence of borderline HC among female subjects was in the Southern and Northern regions, respectively. The prevalence of high HC was higher among female subjects, compared with male subjects across all regions. The highest and lowest prevalence of high HC among male subjects was in the Eastern and Northern regions, respectively, while the highest and lowest prevalence of high HC among female subjects was in the Eastern and Northern regions, respectively.

There was no significant difference between male and female subjects of each region with respect to prevalence of borderline high HC or high HC, in spite of higher

prevalence of high HC among female subjects across all regions.

The prevalence of HC (>5.2 mmol/L) among subjects over the age of 40 years was highest and lowest, 33% and 18.8%, for male subjects of the Eastern and Southern regions, respectively; 29.2% and 17.0% for female subjects of Eastern and Western regions, respectively.

Discussion

This study addresses, from the epidemiological point of view, the issue of serum total and fractionated cholesterol concentration distribution and prevalence of borderline high and high hypercholesterolemia among subjects over the age of 15 years in different regions of Saudi Arabia.

There was a variable pattern of serum total and fractionated cholesterol concentration distribution among Saudi subjects. It appears, however, that, at large, male subjects of the Eastern and Northern regions had higher and lower prevalence of cholesterol-related risk factors for CVD, respectively, compared with male subjects of other regions. Female subjects of the Eastern region and, to a lesser extent, of the Southern region, had higher prevalence of cholesterol-related risk factors for CVD, while female subjects of the Northern region had a lower prevalence of cholesterol-related risk factors for CVD. Male and female subjects over the age of 40 years, in the Eastern region, have the highest prevalence of HC.

There are special demographic and socioeconomic characters for each region of Saudi Arabia, which may contribute to the regional differences in the prevalence of different diseases, among them, hypercholesterolemia. The Eastern region is the oil-producing province with the longest history of adopting the Western lifestyle with respect to nutritional habits and exercise. The Northern region is in close geographical proximity with neighboring countries known for consumption of Mediterranean food, rich with olive oil, with its proven lowering effect on cholesterol.^{14,15} The Southern region is the least urbanized province.

The increase in prevalence of cholesterol-related risk factors for CVD in the Eastern Region can be partially explained by the above-cited factors, especially for subjects of the Eastern and Northern regions. Such factors, however, cannot explain the increase in prevalence of cholesterol-related risk factors among subjects in the Southern regions.

The means and the 90th percentile of serum TCC across all regions and for most of the age groups is lower than the means and the 90th percentile of serum TCC among subjects of Northern and Eastern Europe and is similar to Southern Europe.¹⁶

TABLE 3. Prevalence of hypercholesterolemia among men in different regions of Saudi Arabia.

Region	Age group (year)	Number	Cholesterol (mmol/L)		
			Low-5.2	5.2-6.2	>6.2
West	15-20	166	91.6	4.2	4.2
	21-30	177	87.6	9.6	2.8
	31-40	141	85.1	7.8	7.1
	41-50	77	80.5	7.8	11.7
	51-60	42	66.7	28.6	4.8
	>60	45	77.8	15.6	6.7
	All	648	85.2	9.3	5.6
	>40	164	76.2	15.2	8.5
Central	15-20	134	89.6	6.0	4.5
	21-30	196	80.1	7.1	12.8
	31-40	99	75.8	13.1	11.1
	41-50	75	77.3	13.3	9.3
	51-60	47	74.5	19.1	6.4
	>60	38	71.1	26.3	2.6
	All	589	80.1	10.9	9.0
	>40	160	75.0	18.1	6.9
South	15-20	131	93.1	2.3	4.6
	21-30	159	89.9	3.8	6.3
	31-40	101	80.2	14.9	5.0
	41-50	71	77.5	12.7	9.9
	51-60	42	83.3	11.9	4.8
	>60	36	86.1	11.1	2.8
	All	540	86.5	7.8	5.7
	>40	149	81.2	12.1	6.7
East	15-20	74	91.9	6.8	1.4
	21-30	111	82.9	10.8	6.3
	31-40	62	77.4	8.1	14.5
	41-50	40	72.5	17.5	10.0
	51-60	27	66.7	11.1	22.2
	>60	21	57.1	28.6	14.3
	All	335	79.7	11.3	9.0
	>40	88	67.0	18.2	14.8
North	15-20	40	92.5	2.5	5.0
	21-30	59	100	-	-
	31-40	35	88.6	8.6	2.9
	41-50	21	85.7	9.5	4.8
	51-60	16	68.8	25.0	6.3
	>60	11	81.8	9.1	9.1
	All	182	90.7	6.0	3.3
	>40	48	79.2	14.6	6.3

The prevalence of hypercholesterolemia in any region is lower than the reported prevalence from some other parts of the world, whether developed, such as the US,¹³ or developing countries, such as Turkey.¹⁷

The youth of the Saudi population, with 60% being under 30 years old, could account to some extent for the relative low prevalence of hypercholesterolemia. This prevalence, however, could increase in the near future as the population advances in age and is exposed for a longer time to contributing or precipitating factors, such as newly acquired nutritional habits, obesity and lack of regular exercise.

TABLE 4. Prevalence of hypercholesterolemia among women in different regions of Saudi Arabia.

Region	Age group (year)	Number	Cholesterol (mmol/L)		
			Low-5.2	5.2-6.2	>6.2
West	15-20	167	90.4	6.0	3.6
	21-30	181	81.8	8.3	9.9
	31-40	122	75.4	17.2	7.4
	41-50	90	85.6	7.8	6.7
	51-60	31	77.4	12.9	9.7
	>60	31	80.6	9.7	9.7
	All	622	83.1	9.6	7.2
	>40	152	82.9	9.2	7.9
Central	15-20	129	86.0	7.0	7.0
	21-30	188	76.6	11.2	12.2
	31-40	104	76.0	17.3	6.7
	41-50	67	82.1	6.0	11.9
	51-60	41	75.6	7.3	17.1
	>60	28	89.3	3.6	7.1
	All	557	79.9	10.1	10.1
	>40	136	81.6	5.9	12.5
South	15-20	125	89.6	6.4	4.0
	21-30	187	78.1	16.0	5.9
	31-40	95	78.9	15.8	5.3
	41-50	70	84.3	10.0	5.7
	51-60	47	76.6	10.6	12.8
	>60	36	69.4	19.4	11.1
	All	560	80.9	12.9	6.3
	>40	153	78.4	12.4	9.2
East	15-20	74	81.1	13.5	5.4
	21-30	115	80.0	10.4	9.6
	31-40	63	73.0	17.5	9.5
	41-50	39	69.2	7.7	23.1
	51-60	16	62.5	12.5	25.0
	>60	10	90.0	10.0	–
	All	317	77.0	12.3	10.7
	>40	65	70.8	9.2	20.0
North	15-20	41	97.6	2.4	–
	21-30	62	83.9	8.1	8.1
	31-40	35	85.7	8.6	5.7
	41-50	23	82.6	8.7	8.7
	51-60	15	66.7	26.7	6.7
	>60	13	84.6	15.4	–
	All	189	85.7	9.0	5.3
	>40	51	78.4	15.7	5.9

Finally, there is a need to study the underlying factors for the regional variation with respect to cholesterol-related risk factors, with emphasis on nutritional habits, including the quantity and quality of food, the prevalence of obesity, glucose intolerance and smoking. Identification

of such factors is essential for monitoring the effectiveness of any future plan for combating cholesterol-related risk factors for CVD.

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