Lipids in Health and Disease

RESEARCH

Open Access

Evaluation of the hypercholesterolemia care cascade and compliance with NCEP-ATP III guidelines in Iran based on the WHO STEPS survey

Shirin Djalalinia[1,2†], Sepehr Khosravi[1†], Moein Yoosefi[3†], Sarvenaz Salahi[4], Zahra Shokri Varniab[1], Ali Golestani[1], Nazila Rezaei[1], Ameneh Kazemi[1], Arezou Dilmaghani-Marand[5], Negar Rezaei[1], Erfan Ghasemi[1], Naser Ahmadi[1], Mohammad-Mahdi Rashidi[1], Yosef Farzi[1], Kamyar Rezaee[1], Maryam Nasserinejad[1,6], Sina Azadnajafabad[1], Elham Abdolhamidi[1], Rosa Haghshenas[1,7], Arefeh Alipour Derouei[1], Azadeh Momen Nia Rankohi[1] and Farshad Farzadfar[1,5*]

Abstract

Introduction Noncommunicable diseases (NCDs), particularly cardiovascular disease (CVD), are the leading cause of death worldwide, with hypercholesterolemia being a major risk factor for CVD. This study evaluated the hypercholesterolemia care cascade in Iran—including prevalence, diagnosis, treatment coverage, and effectiveness—using the National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP III) guidelines.

Methods This cross-sectional study drew on data from the 2021 Iran STEPS survey, which employed a systematic cluster sampling of adults aged ≥ 18 years across all provinces in Iran. Hypercholesterolemia was defined per NCEP-ATP III thresholds (LDL ≥ 160 mg/dL, total cholesterol ≥ 240 mg/dL, HDL ≤ 40 mg/dL, or ongoing lipid-lowering therapy). Weighted descriptive statistics were calculated, and Poisson regression with robust variance estimated crude and adjusted prevalence ratios for optimal lipid control among those treated. The 10-year CVD risk was determined using the Framingham Risk Score, stratifying participants into low (< 10%), intermediate (10–20%), and high (> 20%) risk categories.

Results Out of 18,074 participants, 10,582 (55.32%, 95% CI: 54.29–56.35) met NCEP-ATP III criteria for hypercholesterolemia. Among these, only 20.61% (19.55–21.72) were receiving pharmacological treatment. Treatment coverage was notably lower in males (13.15%, 11.98–14.40) than females (29.12%, 27.35–30.96). Statins were the most commonly used medication (11.43% of males, 25.87% of females). Of those receiving treatment, 52.85% (females) and 53.93% (males) achieved optimal LDL, while 76.98% (females) and 81.06% (males) attained total cholesterol < 200 mg/dL. However, only 19.89% (females) and 3.97% (males) met the HDL > 60 mg/dL goal. The 10-year CVD risk was < 10% in 57.79% of participants, 10–20% in 33.27%, and > 20% in 8.94%.

†Shirin Djalalinia, Sepehr Khosravi and Moein Yoosefi equally contributed to this study.

*Correspondence:
Farshad Farzadfar
f-farzadfar@tums.ac.ir
Full list of author information is available at the end of the article

Conclusion Despite a high prevalence of hypercholesterolemia in Iran, treatment coverage remains suboptimal, particularly among males and working-age adults. Although most treated individuals achieve favorable LDL and total cholesterol levels, gaps persist in achieving optimal HDL targets. These findings underscore the need for strengthened screening, treatment, and adherence strategies—alongside broader preventive measures—to reduce the burden of hypercholesterolemia and CVD in Iran.

Keywords Hypercholesterolemia, Cascade of Care, Hypolipidemic Agents, Lipid Metabolism Disorders, Risk Reduction Behavior

Introduction

Noncommunicable diseases (NCDs) are the primary cause of death globally, accounting for a significant proportion of premature mortality and placing considerable strain on health systems, especially in low- and middle-income countries (LMICs) [1, 2]. In support of Sustainable Development Goal (SDG) 3.4, the United Nations has pledged to reduce premature mortality from NCDs by one-third by 2030 [3]. Hypercholesterolemia, a major risk factor for atherosclerosis and cardiovascular disease (CVD), has become increasingly prevalent worldwide, with global morbidity and mortality attributed to high total cholesterol (TC) rising by over 25% in the past decade [4, 5]..

The National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP III) is a widely accepted and recently revised guideline for hypercholesterolemia treatment [6], recommending pharmaceutical therapy for high cholesterol in approximately 43.2 million (37.5%) of U.S. adults [7]. Under these guidelines, individuals with coronary heart disease (CHD) or diabetes who have an LDL level $\geq$ 100 mg/dL are considered definite candidates for statin therapy, with further decisions informed by a 10-year risk assessment for Hard CHD based on the Framingham model [7]. However, despite this monitoring strategy, a considerable number of patients, particularly those at higher risk of CHD, fail to achieve target lipid levels [8–10].

Despite the adoption of the NCEP-ATP III guidelines, the prevalence of hypercholesterolemia in Iran remains notably high, and the cascade of care reveals considerable gaps [11]. According to the 2016 STEPS survey, 80.0% of the Iranian adult population had at least one lipid abnormality, including 69.2% with low HDL-C, 39.5% with high non–HDL-C, 28.0% with hypertriglyceridemia, and 26.7% with hypercholesterolemia [5]. Among those with hypercholesterolemia, 74.2% were aware of their condition; however, only 36.5% achieved the desired LDL-C levels [12]. These findings underscore a critical unmet need, especially for high-risk individuals, and highlight the importance of understanding the full hypercholesterolemia care continuum in Iran to improve management according to NCEP-ATP III guidelines.

More broadly, hypercholesterolemia is a major modifiable risk factor for CVD in LMICs, where substantial unmet needs persist due to limited health system capacity [11]. his gap is evident across all stages of care—from inadequate screening and diagnosis to insufficient treatment and control—contributing to poor outcomes and increased cardiovascular risk. Previous research has emphasized the urgency of addressing these deficiencies and the necessity for detailed, nationally representative data to guide effective health system responses [13]. In the context of Iran, as an LMIC in the Eastern Mediterranean region, comprehensive insights into the diagnosis, treatment coverage, and treatment effectiveness of hypercholesterolemia are essential for shaping robust CVD prevention strategies.

Therefore, the aim of this study was to estimate the national and sub-national diagnosis, treatment coverage, and treatment effectiveness of hypercholesterolemia pharmaceutical therapies in Iran, based on the therapeutic targets and strategies of the NCEP-ATP III guidelines. This focus is particularly important because hypercholesterolemia is on the rise in LMICs, including in the Eastern Mediterranean region, yet there is a substantial unmet need for hypercholesterolemia care, with suboptimal performance across all stages of the care cascade. Detailed evidence is urgently needed to guide health systems in responding to this epidemic. The findings of this study could enhance the understanding of hypercholesterolemia diagnosis, treatment coverage, and treatment effectiveness in the Iranian population, providing valuable insights for policymakers to help prevent cardiovascular events. Additionally, it offers 10-year risk estimates for CHD among the Iranian population, further informing strategic interventions to mitigate the growing burden of CVD.

Methods

Overview

This cross-sectional study utilized data from the Iran STEPS Survey 2021. Comprehensive details of the Iran STEPS Survey 2021 are provided elsewhere in a study protocol [14]. This survey, conducted from the second week of January 2021 to the last week of March 2021,

had three phases of data collection via questionnaires, anthropometric measurements, and laboratory assessments. The first phase of the survey was designed based on the latest version of the WHO STEPS instrument, version 3.2 [15]. Additionally, some questions were added to the survey based on national needs.

Survey sampling and population

To ensure national and subnational representativeness, a systematic clustered sampling method was used to recruit Iranian adults aged ≥ 18 years from both urban and rural areas across all 31 provinces of Iran. The 2021 STEPS survey included 28,821 individuals, of whom 27,874 completed the first phase (questionnaire step), 27,745 completed the second phase, and 18,119 completed the third phase. The third phase involved a drop in sample size, as it included only individuals aged ≥ 25 years, in line with the STEPS framework. More detailed information about the study population and the sampling method for the 2021 STEPS survey can be found in a separate publication [14]. The current study includes 18,074 individuals, excluding those with missing values for lipid profile components (LDL, HDL, TG, total cholesterol) or antilipid medication data.

Data collection

In Phase Two of the STEPS Study, participants underwent comprehensive physical assessments, including height, weight, waist and hip circumferences, blood pressure, and pulse rate. Blood pressure was measured three times on the brachial artery using standard Beurer sphygmomanometers, with each reading taken three minutes apart after the participant had rested for 15 min in a seated position. The final blood pressure value was calculated as the average of the second and third measurements. Height was measured with a standard meter while the participant stood straight against a wall, ensuring that the heels, hips, and back of the head were aligned. Weight was recorded using a calibrated digital scale (Inofit), which was checked with a 5 kg index scale each time the device was moved. These standardized measurements were performed for all eligible participants during the second phase of the study.

Sample collection followed a detailed protocol starting with participant recruitment and the allocation of unique barcodes. Blood samples were collected and underwent primary processing, including centrifugation, aliquoting, and temporary storage at 2–8°C. Transportation of samples to the central laboratory was conducted in vaccine transport boxes maintained at 4°C, with digital thermometers continuously monitoring the temperature to ensure sample integrity. The entire process, from collection to the central lab, was managed within 18 h to maintain quality. At the central lab, biochemical tests were conducted using the Roche-Hitachi Cobas C311 auto-analyzer, which included assessments of serum total cholesterol, HDL-C, triglycerides, HbA1c, and fasting plasma glucose. After testing, results were automatically sent to the server and validated through laboratory process management software (LabIt), with any discrepancies addressed through retesting. This comprehensive protocol ensured the accurate and efficient collection, transportation, and analysis of biological samples [14].

Hypercholesterolemia cascade of care variables

The primary outcomes of this study are the components of the care cascade, as defined by the NCD Risk Factor Collaboration (NCD-RisC) studies and outlined below [16]:

Hypercholesterolemia (HC) Diagnosis

Hypercholesterolemia diagnosis (HC), according to the NCEP-ATP III guidelines, is defined as LDL levels greater than or equal to 160 mg/dL, total cholesterol (TC) levels greater than or equal to 240 mg/dL, HDL levels less than or equal to 40 mg/dL, or receiving medication for hypercholesterolemia [17].

Treatment coverage of HC

Coverage of hypercholesterolemia treatment was defined as a positive response to the question, 'Because of your high cholesterol, are you now taking prescribed medicine?' among individuals who had HC.

Effectiveness of treatment

Effectiveness of HC treatment was defined as meeting NCEP/ATP III guideline levels for TC and LDL-C among those who were HC treated. In Table 1 we present the LDL-C goals recommended by NCEP ATP II and ATP III criteria based on the presence of CHD, CHD risk factors, and CHD risk equivalents. We did not have complete data about CHD (clinical CHD, symptomatic carotid artery disease, peripheral arterial disease, and abdominal aortic aneurysm) so we only included clinical CHD and we replaced the underlying diabetes instead of CHD as CHD risk equivalent [17]. CHD risk factors consist of current cigarette smoking, hypertension, low HDL cholesterol (< 40 mg/dL), family history of premature coronary heart disease CHD, and age (males > 45 years; females > 55 years) [18].

Framingham hard CHD 10-year risk in individuals with hypercholesterolemia

For the secondary outcomes, we also assess the Framingham Hard CHD 10-Year Risk. The Framingham Hard CHD 10-Year Risk is a predictive model developed from

Table 1 LDL cholesterol goals and cut points for Therapeutic Lifestyle Changes (TLC) and drug therapy in different risk categories (Major risk factors (Exclusive of LDL Cholesterol) That modify LDL goals:

Risk Category	LDL Goal (mg/dL)	LDL Level to Initiate Therapeutic Lifestyle Changes (TLC) (mg/dL)	LDL Level to Consider Drug Therapy (mg/dL)
CHD or CHD Risk Equivalents (10-year risk > 20%)	< 100	> = 100	> = 130 (100–129: drug optional)[a]
2 + Risk Factors (10-year risk ≤ 20%)	< 130	> = 130	10-year risk 10–20%: > = 130, 10-year risk < 10%: > = 160
0–1 Risk Factor	< 160	> = 160	> = 190 (160–189: LDL-lowering drug optional)

[a] Note: HDL cholesterol ≥ 60 mg/dL counts as a "negative" risk factor; its presence removes one risk factor from the total count

1. Cigarette smoking

2. Hypertension (BP ≥ 140/90 mmHg or on antihypertensive medication)

3. Low HDL cholesterol (< 40 mg/dL)[a]

4. Family history of premature CHD (CHD in male first-degree relative < 55 years; CHD in female first-degree relative < 65 years), and

5. Age (males ≥ 45 years; females ≥ 55 years)

the Framingham Heart Study to estimate the probability of developing "hard" CHD events, such as myocardial infarction and coronary death, over a 10-year period [17, 18]. According to the NCEP Adult ATP III Guidelines, this risk assessment is a cornerstone for managing lipid disorders and assessing cardiovascular risk. The model incorporates key variables, including age and sex, as risk increases with age and differs between genders. Total cholesterol and HDL cholesterol levels are crucial lipid measures included in the risk calculation. Systolic blood pressure, both treated and untreated, is another important factor, reflecting the impact of hypertension on CHD risk. Cigarette smoking is considered a risk factor and is included in the assessment, as is the presence of diabetes mellitus, which is regarded as a CHD risk equivalent under ATP III guidelines. Based on the calculated risk, individuals are categorized into low (< 10%), intermediate (10–20%), or high (> 20%) risk groups, guiding the implementation of lifestyle interventions and pharmacologic treatments, such as statin therapy, for CHD prevention.

Definition of covariates

We included a comprehensive set of demographic and clinical characteristics as potential covariates in the analysis. These variables encompassed age, residence area (rural/urban), province of residence, marital status, years of schooling, employment status, health insurance coverage (basic or complementary), and wealth index (WI). In Iran, basic health insurance is mandated for nearly all citizens, providing universal coverage of essential healthcare services, while complementary insurance options offer expanded benefits or higher reimbursements for specialized treatments. Physical activity was assessed based on MET scores using the Global Physical Activity Questionnaire (GPAQ), with a score above 600 classified as appropriate. Additional variables included current cigarette smoking (any use within the last 12 months), diabetes mellitus (defined as fasting blood glucose ≥ 126 mg/dl or current use of oral agents or insulin), and hypertension (systolic blood pressure ≥ 140 mmHg, diastolic blood pressure ≥ 90 mmHg, or current use of antihypertensive medication) [19, 20].

Further factors considered were the history of ever visiting a traditional healer for high cholesterol, current use of traditional medicine for high cholesterol, family history of heart attack, stroke, or sudden death, familiarity with and adherence to the traffic light food guide, frequency of adding salt during meals, and the perceived importance of salt reduction. Overweight was defined as a BMI ≥ 25 kg/m^2. The wealth index (WI) was calculated using a structured questionnaire that assessed household assets through 36 questions across various asset dimensions. Principal component analysis (PCA) was applied to summarize the data, with the first principal component, containing the largest variance, designated as the WI. This index was divided into five quintiles, ranging from the poorest (first quintile) to the wealthiest (fifth quintile).

Lipid-lowering medications were categorized into four groups: Statins (HMG-CoA reductase inhibitors, such as atorvastatin and simvastatin), Bile Acid Sequestrants (BAS) (e.g., cholestyramine and colesevelam), Nicotinic Acid (NA) (e.g., niacin), and Unknown (medications for which participants were unable to provide or recall the name).

Statistical analysis

Weighted prevalence, mean, and standard deviation (SE) were used to describe the data. 95% confidence interval (95% CI) for each quantitative variable was reported. The weighting procedure in this survey, conducted after cleaning the gathered data, consisted of four stages. First, weighting for overall non-response addressed individuals who refused to participate,

especially considering the impact of the COVID-19 outbreak, with specific calculations for different age groups. Second, non-response weighting was applied at each survey phase, using equations to mitigate data loss and measurement bias from incomplete responses. Third, samples from each province were weighted based on age, sex, and area of residence to ensure representativeness across demographics. For further details on the weighting process, please refer to the study protocol [14].

For the regression analyses, we employed Poisson regression with robust variance estimation to estimate prevalence ratios (PRs) for optimal treatment achievement (Yes/No). Initially, all available variables were assessed in univariate (crude) Poisson regression models. Based on these univariate analyses, only those variables with a p-value < 0.2 were included in the final adjusted model, which was used to estimate adjusted PRs and corresponding 95% CIs. This approach allowed us to focus on the most relevant predictors while maintaining model parsimony.

To assess model assumptions and overall fit, we computed several diagnostic metrics. The residual deviance and degrees of freedom were examined alongside the Pearson chi-square statistic. The dispersion ratio—calculated as the Pearson chi-square divided by the residual degrees of freedom—was used to evaluate the equidispersion assumption, with values near 1 indicating an acceptable fit. Additionally, the Akaike Information Criterion (AIC) was computed for model comparison purposes, bearing in mind that its interpretation in quasi-Poisson models (which are based on quasi-likelihood) should be approached with caution.

Predictive performance was evaluated using ten-fold cross-validation. For each fold, the mean absolute error (MAE) and root mean squared error (RMSE) were calculated to assess the model's ability to generalize to unseen data. These metrics provided an objective measure of the model's predictive accuracy.

All data analyses were conducted using R statistical package version 4.4.0 and "Survey" Package and the caret package for cross-validation [21–24]. P-value less than 0.05 was considered as statistically significant. The analysis was conducted using complete case data, including only observations with no missing values.

Ethical consideration.

The research protocol for the study was approved by the Research Ethics Committees of the Endocrine & Metabolism Research Institute at Tehran University of Medical Sciences, with the approval number IR.TUMS.EMRI.REC.1402.017.

Results

Population characteristics

A total of 18,074 participants were included in this study. The mean ages of male and female participants were 48.97 (95% CI: 48.50–49.45) years and 47.69 (95% CI: 47.28–48.09) years, respectively. Most participants were married (76.6%), had more than 12 years of schooling (43.7%), resided in urban areas (75.0%), and were covered by basic insurance (89.6%). The results of the study revealed that, at the national level, the mean levels of TC, LDL, and HDL were 171.99 mg/dL (95% CI: 171.18–172.80), 99.51 mg/dL (95% CI: 99.81–100.21), and 42.23 mg/dL (95% CI: 42.02–42.43), respectively (Table 2).

Cascade of care

Hypercholesterolemia diagnosis

Out of 18,074 participants, 10,582 individuals were diagnosed with hypercholesterolemia and were eligible for treatment according to the National Cholesterol Education Program ATP III guidelines. The national prevalence of hypercholesterolemia was 55.32% (95% CI: 54.29–56.35) for both sexes among the total sample of 18,074 individuals. The prevalence was higher among males (66.73%, 95% CI: 65.33–68.21) compared to females (46.56%, 95% CI: 45.19–47.93) and varied across age groups, with the highest prevalence observed in individuals aged 55–59 years. Urban residents had a slightly higher prevalence compared to rural residents. Additionally, individuals with no formal education had the highest prevalence. Refer to Table 3 for more details.

Coverage

Among individuals with hypercholesterolemia (10,582 individuals), the overall treatment coverage was 20.61% (95% CI, 19.55–21.72). Treatment coverage was 13.15% (95% CI, 11.98–14.40) in males and 29.12% (95% CI, 27.35–30.96) in females. Treatment coverage seems to increase in line with the increasing of age, as in the age group of 55 years and above, it reaches to more than 20%. In terms of employment status, the least medical coverage was related to the working group (5.6%, 95% CI: 4.95–6.35), and in terms of marital status, it belonged to people who were single (3.19%, 95% CI: 1.8–5.65). (Supplementary Table 1). The majority of coverage for both males and females were achieved through the statin group. The highest coverage was observed in females from Gilan at 44%, while the lowest was in females from West Azerbaijan at 3.5% (Fig. 1).

Treatment effectiveness

A total of 2,758 individuals were receiving treatment. Significant differences were observed in the serum

Table 2 Baseline Table based on receiving medication

Variable	Group	Medication	No Medication	*P*_value	Total
Sex	Female	13.46 (12.59–14.4)	86.54 (85.6–87.41)	< 0.001	10,267 (56.81%)
Sex	Male	8.71 (7.93–9.56)	91.29 (90.44–92.07)	< 0.001	7807 (43.19%)
Residential of area	Rural	9.84 (8.97–10.79)	90.16 (89.21–91.03)	< 0.001	5853 (32.38%)
Residential of area	Urban	11.85 (11.1–12.64)	88.15 (87.36–88.9)	< 0.001	12,221 (67.62%)
Age group	25–29	0.88 (0.29–2.62)	99.12 (97.38–99.71)	< 0.001	1480 (8.19%)
Age group	30–34	1.4 (0.86–2.27)	98.6 (97.73–99.14)	< 0.001	2057 (11.38%)
Age group	35–39	2.78 (2.08–3.7)	97.22 (96.3–97.92)	< 0.001	2282 (12.63%)
Age group	40–44	4.96 (3.9–6.28)	95.04 (93.72–96.1)	< 0.001	2173 (12.02%)
Age group	45–49	8.64 (7.21–10.31)	91.36 (89.69–92.79)	< 0.001	2141 (11.85%)
Age group	50–54	15.29 (13.35–17.45)	84.71 (82.55–86.65)	< 0.001	1948 (10.78%)
Age group	55–59	20.06 (17.61–22.75)	79.94 (77.25–82.39)	< 0.001	1765 (9.77%)
Age group	60–64	23.83 (21.06–26.84)	76.17 (73.16–78.94)	< 0.001	1536 (8.5%)
Age group	65 and above	23.94 (21.75–26.28)	76.06 (73.72–78.25)	< 0.001	2692 (14.89%)
Years of schooling	0	20.4 (18.67–22.24)	79.6 (77.76–81.33)	< 0.001	3172 (17.66%)
Years of schooling	1–7	15.63 (14.3–17.06)	84.37 (82.94–85.7)	< 0.001	5043 (28.08%)
Years of schooling	7–12	9.43 (8.08–10.99)	90.57 (89.01–91.92)	< 0.001	3360 (18.71%)
Years of schooling	12 +	6.36 (5.61–7.21)	93.64 (92.79–94.39)	< 0.001	6382 (35.54%)
Employment group	Worker	5.62 (4.96–6.36)	94.38 (93.64–95.04)	< 0.001	6522 (36.32%)
Employment group	Retired	20.19 (17.62–23.03)	79.81 (76.97–82.38)	< 0.001	1728 (9.62%)
Employment group	Unemployed	8.79 (6.82–11.26)	91.21 (88.74–93.18)	< 0.001	907 (5.05%)
Employment group	Unpaid	14.39 (13.42–15.41)	85.61 (84.59–86.58)	< 0.001	8800 (49.01%)
Marriage Status	Single	3.21 (1.8–5.65)	96.79 (94.35–98.2)	< 0.001	1417 (7.84%)
Marriage Status	Married	11 (10.36–11.68)	89 (88.32–89.64)	< 0.001	15,047 (83.25%)
Marriage Status	Divorced	7.94 (5.06–12.24)	92.06 (87.76–94.94)	< 0.001	400 (2.21%)
Marriage Status	Widow	27 (23.79–30.46)	73 (69.54–76.21)	< 0.001	1210 (6.69%)
LDL		85.70 (83.97–87.60)	101.23 (100.49–101.97)	< 0.001	
Cholestrol		162.50(160.22–164.79)	173.16(172.30–174.01)	< 0.001	
HDL		41.73(41.10–42.37)	42.29(42.07–42.51)	< 0.001	

levels of LDL (85.7%, 95% CI 83.79–87.6 vs. 101.23%, 95% CI 100.49–101.97) and cholesterol (162.5%, 95% CI 160.22–164.79 vs. 173.16%, 95% CI 172.3–174.01) between people who were under medication and those who did not receive any medical intervention ($p < 0.001$) (Table 1). In both males and females, the most used type of medication was the statins group, with 7.61% (95% CI 6.91–8.41) and 12.01% (95% CI 11.21–12.93), respectively. The predominance of HMG CoA reductase inhibitors (statins) was evident across nearly all demographic groups (Supplementary Table 2). Specifically, females showed a higher statin usage (12.01%, 95% CI: 11.21–12.93) than males (7.61%, 95% CI: 6.91–8.41). Urban residents also had somewhat higher statin use (10.46%, 95% CI: 9.78–11.24) compared to their rural counterparts (8.83%, 95% CI: 8.02–9.75). Examining age groups, statin use rose steadily from only 0.87% (95% CI: 0.29–2.62) among 25–29 year-olds to 21.73% (19.67–24.03) among those aged ≥ 65. When analyzed by educational level, individuals with no schooling had the highest statin use (17.85%, 95% CI: 16.32–19.62), whereas those with ≥ 12 years of schooling reported lower usage (5.61%, 95% CI: 4.93–6.42). Among employment categories, retired participants had the greatest statin coverage (18.22%, 95% CI: 15.80–20.92), while employed workers reported only 4.93% (4.32–5.64). Statin usage also varied with marital status, from a low of 2.95% (1.60–5.44) among single individuals to 24.63% (21.53–28.01) among widowed participants.In contrast, use of bile acid sequestrants or nicotinic acid alone was rare (< 1%) in most subgroups. Combination therapies (e.g., bile acid + nicotinic acid, or triple therapy) were scarcely reported in any demographic category, generally at or below 0.1%.

Among individuals receiving treatment for hypercholesterolemia, optimal treatment was achieved in 52.85% (51.47–54.23) of females and 53.93% (52.35–55.51) of males based on LDL levels, 76.98% (75.75–78.14) of females and 81.06% (79.78–82.28) of males based on total cholesterol levels, and 19.89% (18.31–21.57) of females

Table 3 Prevalence of hypercholesterolemia diagnosis based on the NCEP ATP III guidelines across demographic variables

Variable	Group	Prevalence (%)	95% CI (%)	*P*_value
Age Group	25–29	46.15	42.26 – 50.04	< 0.001
	30–34	53.63	50.32 – 56.94	
	35–39	51.12	48.44 – 53.81	
	40–44	53.05	50.22 – 55.88	
	45–49	54.76	51.74 – 57.78	
	50–54	55.64	52.68 – 58.61	
	55–59	61.2	58.22 – 64.19	
	60–64	59.91	55.83 – 63.99	
	65 and above	60.75	58.29 – 63.21	
Sex	Male	66.73	65.33 – 68.21	< 0.001
	Female	46.56	45.19 – 47.93	
Area	Rural	53.04	51.51 – 54.57	0.001
	Urban	56.31	55.00 – 57.63	
Education Level	0 Years	57.85	55.44 – 60.26	0.03
	1–7 Years	56.13	53.74 – 58.52	
	7–12 Years	55.68	53.56 – 57.80	
	> 12 Years	53.68	51.50 – 55.86	
Wealth Index	Poorest (1)	54.1	51.85 – 56.35	0.74
	Second (2)	55.67	53.38 – 57.95	
	Middle (3)	56.13	54.04 – 58.21	
	Fourth (4)	55.66	53.45 – 57.87	
	Richest (5)	56.16	53.40 – 58.92	

and 3.97% (3.35–4.70) of males based on HDL levels (Supplementary Table 1).

Optimal treatment was most prevalent among individuals aged 25–29, those with 7–11 years of schooling, employed individuals, singles, diabetics, normotensive, smokers, and underweight individuals. Ineffective treatment was more common among individuals aged 55–59, illiterate, unpaid workers, widowed, non-diabetic, hypertensive, non-smokers, and those with normal or higher weight (Table 2).

Restriction of salty foods, as a decreasing risk factor, and tobacco smoking, as a potential increasing factor, were significantly associated with desirable lipid profile components ($p < 0.001$) (Supplementary Tables 2–3).

Effectiveness of treatment, measured via ATP III criteria for LDL < 130 mg/dL, total cholesterol < 200 mg/dL, and HDL > 60 mg/dL, was assessed using adjusted prevalence ratios (aPR) from the final models (Supplementary Tables 5). In brief, being unemployed was positively associated with achieving LDL < 130 mg/dL (aPR = 2.10, 95% CI: 1.09–4.04), whereas having diabetes (aPR = 0.71, 95% CI: 0.51–0.99) or currently smoking (aPR = 0.65, 95% CI: 0.47–0.91) reduced the likelihood of LDL control. For total cholesterol < 200 mg/dL, retired participants had lower odds (aPR = 0.50, 95% CI: 0.29–0.87) than workers, and both diabetes (aPR = 0.68, 95% CI: 0.52–0.88) and smoking (aPR = 0.74, 95% CI: 0.58–0.95) again showed negative impacts.

In adjusted analyses, key determinants of lipid control included several modifiable factors. For LDL (< 130 mg/dL), unemployed individuals had significantly higher odds of achieving target levels (aPR = 2.10, 95% CI: 1.09–4.04), whereas diabetes (aPR = 0.71, 95% CI: 0.51–0.99) and current tobacco smoking (aPR = 0.65, 95% CI: 0.47–0.91) were associated with lower odds of control. In terms of total cholesterol (< 200 mg/dL), retired participants had lower odds compared with workers (aPR = 0.50,

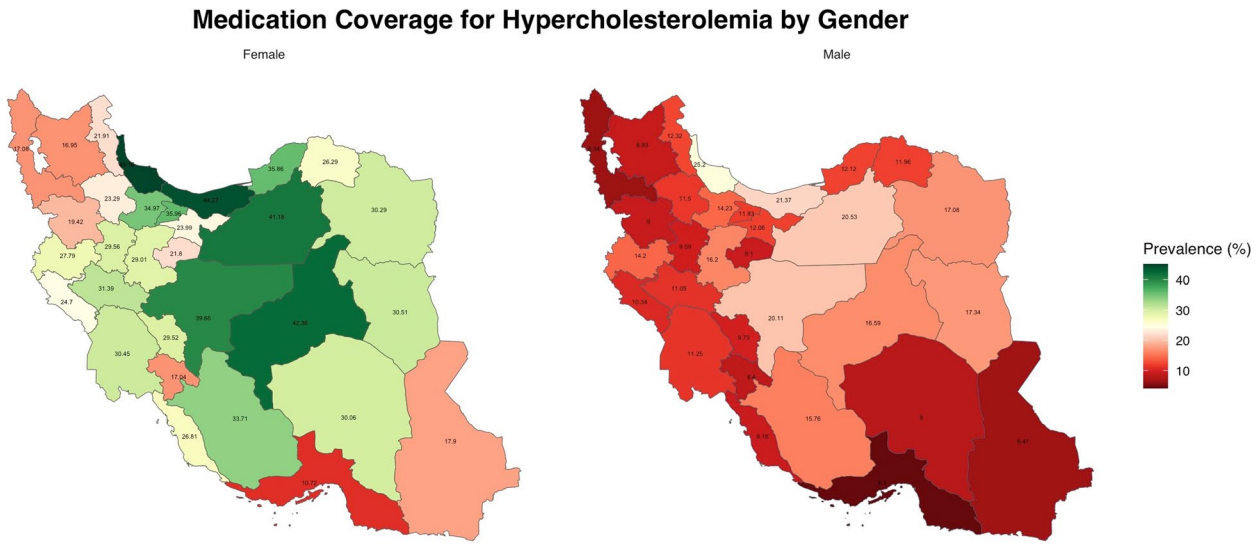

Fig. 1 Medication coverage based on NCEP/ATP III guidelines by sex at subnational level

95% CI: 0.29–0.87), with both diabetes (aPR = 0.68, 95% CI: 0.52–0.88) and smoking (aPR = 0.74, 95% CI: 0.58–0.95) similarly reducing the likelihood of meeting the target. For HDL (> 60 mg/dL), being male was independently linked to a lower probability of optimal levels (aPR = 0.38, 95% CI: 0.30–0.48). For full details, please refer to Table 4

Treatment effectiveness based on risk factors Among those with senility (males ≥ 45 years or females ≥ 55 years), 48.41% (95% CI: 46.81–50.01) had optimal LDL levels (< 100 mg/dL), while 31.2% (95% CI: 29.74–32.69) had LDL levels between 100–129 mg/dL. Only 0.88% (: 0.68–1.13) had very high LDL levels (≥ 190 mg/dL). For individuals with a family history of CHD (male < 55 years, female < 65 years), 53.6% (95% CI: 50.71–56.46) achieved optimal LDL levels, while 1.55% (95% CI: 0.7–3.4) had very high LDL levels. Among current cigarette smokers, 56.84% (95% CI: 53.35–60.26) had optimal LDL levels, with only 0.48% (95% CI: 0.25–0.93) showing very high LDL. In individuals with hypertension, 51.47% (95% CI: 49.71–53.24) had optimal LDL levels, while 1.07% (95% CI: 0.83–1.38) had very high LDL levels. When stratified by risk factor frequency, 53.93% (95% CI: 52.68–55.18) of individuals with 0–1 risk factors had optimal LDL levels, while 52.05% (95% CI: 50.19–53.89) of those with ≥ 2 risk factors had optimal LDL levels. Among those with ≥ 2 risk factors, 1.05% (95% CI: 0.8–1.37) had very high LDL levels.

10-Year hard CHD risk assessment in individuals with hypercholesterolemia

Using the available data for CHD risk factors, and CHD risk equivalents and following the Framingham risk scoring approach, the geographical patterns of distribution of high CVD risk patients (> 20%) for chance of having a heart attack or stroke in the next 10 years, was mostly concentrated in the northwestern provinces. For both males and females, Yazd province had a high prevalence of high-risk patients. The lowest risk (< 10%) was seen in the southeastern region and specifically in the Sistan and Baluchistan province (Fig. 2). At national level in males, 80.02 (95% CI: 73.64–85.16) have more than 20% risk of 10-year CHD event. The same number for females is 8.94 (5.99–13.15). The 10-year risk CHD was also assessed for the total population, encompassing both males and females. The majority of participants were classified as having a low 10-year risk (< 10%), with a prevalence of 57.79% (52.96–62.48). A moderate risk (10–20%) was observed in 33.27% (29.11–37.71) of the population, while a high risk (> 20%) was noted in 8.94% (5.99–13.15). The differences in CHD risk categories were statistically significant ($p < 0.001$).

Discussion

This study found that hypercholesterolemia is more common in males (66.73%) than females (46.56%), with the highest prevalence in individuals aged 55 to 59 years (61.2%). Among those diagnosed, only 20.61% received treatment, with significantly lower coverage in males (13.15%) compared to females (29.12%). Treatment rates increased with age but were lowest among working individuals (5.6%) and single individuals (3.19%). Most treated patients were prescribed statins. Regional disparities were significant, with the highest treatment coverage in females from Gilan Province (44%) and the lowest in females from West Azerbaijan Province (3.5%). Despite guidelines recommending treatment for 41.6% of adults, a substantial treatment gap remains, underscoring the need for targeted interventions focused on males, younger populations, working individuals, and regions with low coverage rates.

More importantly, this study revealed a striking 60% gap between hypercholesterolemia diagnosis and treatment coverage, consistent with previous national reports [12]. This disparity underscores a critical unmet need for hypercholesterolemia care, particularly in LMIC, where resource limitations further exacerbate care deficiencies. Consistent with prior studies, we found that only 1 in 5 individuals meeting treatment criteria receives appropriate therapy. Although this reflects some alignment with WHO guidance on targeting high-risk individuals for screening, a deeper analysis reveals persistent gaps in the care cascade [11]. Despite the high prevalence of hypercholesterolemia and its strong association with other CVDs risk factors, treatment rates did not improve significantly among individuals with additional comorbidities. This highlights a systemic failure to prioritize high-risk individuals in screening and treatment efforts. These findings suggest that existing healthcare frameworks inadequately address the multifactorial nature of hypercholesterolemia and its associated risks. Enhancing the integration of hypercholesterolemia management with broader CVD prevention programs and strengthening health systems to deliver equitable, comprehensive care are imperative to bridging this gap.

Our study also found that 8 out of 10 Iranian males over the age of 25 have a more than 20% risk of a cardiovascular event in the next ten years, which is alarmingly high compared to about 1 in 10 females in the same age group, highlighting a sex disparity. This disparity could, to some extent, be attributed to differences in cigarette smoking and lipid profiles, as also reflected in the treatment coverage [2, 25]. This considerably higher than countries in the middle east region like Egypt with similar population size to Iran (with 58% at risk of CHD) which could be contributed to aging population of Iran compared to Egypt [26].

Table 4 Associates of desirable LDL level of below 130, total cholesterol level of below 200, and HDL level of above 60 according to ATP III classification

Variable	PR (95% CI) Crude	Adjusted PR (95% CI)	PR (95% CI) Crude	Adjusted PR (95% CI	PR (95% CI) Crude	Adjusted PR (95% CI)
Total Cholesterol			**HDL**		**LDL**	
Sex	0.7 (0.54, 0.9)	0.69 (0.43, 1.13)	0.42 (0.35, 0.5)	0.38 (0.3, 0.48)	0.69 (0.49, 0.96)	0.71 (0.39, 1.3)
Residential area	0.9 (0.7, 1.15)	-	1.02 (0.9, 1.14)	0.96 (0.84, 1.09)	0.74 (0.54, 1.02)	-
Age group (30–34) Reference (25–29)	2.58 (0.27, 24.86)	-	0.61 (0.32, 1.16)	-	0.72 (0.09, 5.57)	-
Age group (35–39)	2.13 (0.24, 18.57)	-	0.39 (0.22, 0.7)	-	0.64 (0.11, 3.85)	-
Age group (40–44)	2.78 (0.33, 23.51)	-	0.55 (0.34, 0.89)	-	1 (0.19, 5.36)	-
Age group (45–49)	2.91 (0.35, 24.09)	-	0.56 (0.35, 0.87)	-	1 (0.19, 5.2)	-
Age group (50–54)	2.27 (0.28, 18.71)	-	0.6 (0.39, 0.91)	-	0.65 (0.13, 3.35)	-
Age group (55–59)	2.2 (0.27, 18.07)	-	0.63 (0.42, 0.96)	-	0.84 (0.17, 4.26)	-
Age group (60–64)	1.64 (0.2, 13.65)	-	0.67 (0.44, 1.02)	-	0.48 (0.09, 2.55)	-
Age group (65 and above)	1.39 (0.17, 11.46)	-	0.7 (0.47, 1.05)	-	0.52 (0.1, 2.63)	-
Marriage status	0.9 (0.77, 1.06)	-	1.03 (0.96, 1.11)	-	0.86 (0.7, 1.06)	-
Employment group (retired) Reference: Worker	0.4 (0.25, 0.63)	0.5 (0.29, 0.87)	1.26 (0.95, 1.67)	1.05 (0.8, 1.39)	0.38 (0.2, 0.71)	0.6 (0.29, 1.25)
Employment group (unemployed)	1.37 (0.79, 2.36)	1.48 (0.85, 2.59)	1 (0.64, 1.56)	0.75 (0.45, 1.25)	2.06 (1.1, 3.84)	2.1 (1.09, 4.04)
Employment group (unpaid)	1.05 (0.79, 1.38)	0.87 (0.54, 1.4)	2.05 (1.65, 2.53)	0.98 (0.77, 1.24)	1.16 (0.8, 1.68)	1.04 (0.55, 1.97)
Years of Schooling (1–7) Reference: 0	0.93 (0.7, 1.25)	-	0.93 (0.82, 1.06)	-	0.79 (0.54, 1.17)	0.72 (0.49, 1.06)
Years of Schooling (7–12)	0.97 (0.67, 1.4)	-	0.81 (0.66, 1)	-	0.79 (0.48, 1.28)	0.81 (0.48, 1.36)
Years of Schooling (12 +)	0.81 (0.58, 1.13)	-	0.86 (0.73, 1.01)	-	0.72 (0.47, 1.11)	0.73 (0.38, 1.38)
WI_National 2 Reference (Wealth Index 1)	0.97 (0.69, 1.36)	-	0.98 (0.82, 1.17)	1.02 (0.86, 1.21)	1.01 (0.66, 1.56)	-
WI_National3	1.11 (0.78, 1.57)	-	0.88 (0.73, 1.05)	1.04 (0.87, 1.24)	1.12 (0.7, 1.78)	-
WI_National4	1 (0.7, 1.42)	-	0.93 (0.78, 1.1)	1.07 (0.89, 1.28)	0.77 (0.46, 1.29)	-
WI_National5	0.63 (0.4, 0.98)	-	1.09 (0.91, 1.3)	1.18 (0.98, 1.43)	0.67 (0.39, 1.15)	-
Basic health insurance	0.94 (0.56, 1.6)	-	1.04 (0.8, 1.35)	-	0.73 (0.4, 1.31)	-
Complementary health insurance	0.68 (0.53, 0.87)	0.95 (0.72, 1.23)	1.06 (0.95, 1.19)	0.98 (0.87, 1.11)	0.63 (0.45, 0.89)	-
Bile Acid (Reference: HMG COA Reductase)	1.22 (0.57, 2.58)	1.24 (0.53, 2.88)	0.68 (0.4, 1.14)	0.96 (0.58, 1.61)	1.77 (0.78, 4.03)	1.98 (0.8, 4.93)
Nicotinic Acid	1.81 (0.67, 4.92)	1.68 (0.58, 4.85)	1.42 (0.97, 2.07)	1.29 (0.94, 1.77)	1.8 (0.49, 6.67)	1.46 (0.29, 7.48)
Unknown	2.18 (1.6, 2.97)	1.76 (1.29, 2.4)	0.61 (0.46, 0.8)	0.65 (0.5, 0.84)	2.34 (1.53, 3.59)	2.09 (1.41, 3.11)
Ever visited traditional healer for high cholesterol	1.21 (0.82, 1.78)	-	0.94 (0.75, 1.18)	1.04 (0.83, 1.31)	0.89 (0.5, 1.57)	-
Current use traditional remedy for high cholesterol	1.3 (0.92, 1.85)	-	0.93 (0.77, 1.12)	0.93 (0.77, 1.11)	1.44 (0.9, 2.29)	-
Diabetes	0.6 (0.47, 0.75)	0.68 (0.52, 0.88)	1.02 (0.9, 1.15)	1.07 (0.95, 1.19)	0.6 (0.44, 0.81)	0.71 (0.51, 0.99)
Current tobacco smoking	0.71 (0.56, 0.89)	0.74 (0.58, 0.95)	0.82 (0.73, 0.92)	0.82 (0.73, 0.91)	0.59 (0.43, 0.82)	0.65 (0.47, 0.91)

Table 4 (continued)

Variable	PR (95% CI) Crude	Adjusted PR (95% CI)	PR (95% CI) Crude	Adjusted PR (95% CI	PR (95% CI) Crude	Adjusted PR (95% CI)
Hypertension Sys > = 140 or dias > = 90 or drug usage	0.91 (0.58, 1.42)	-	0.5(0.35, 0.71)	0.89(0.6, 1.34)	0.49(0.24, 1.01)	-
Experience of heart attack or stroke or sudden death in family	0.8 (0.62, 1.02)	-	0.92 (0.82, 1.04)	-	0.85 (0.61, 1.17)	-
Low physical activity	1.03 (0.77, 1.37)	-	0.99 (0.85, 1.15)	-	1 (0.69, 1.45)	-
BMI (25–30) (Reference: Under 25)	1.04 (0.82, 1.32)	-	1.09 (0.97, 1.23)	-	1.13 (0.82, 1.55)	-
BMI (30–35)	1.13 (0.78, 1.64)	-	0.84 (0.72, 0.99)	-	1.04 (0.64, 1.68)	-
BMI (more than 35)	1.02 (0.69, 1.5)	-	0.8 (0.67, 0.95)	-	0.9 (0.55, 1.5)	-
Familiar with traffic light guide to food	1.28 (0.81, 2.01)	-	0.95 (0.78, 1.15)	-	1.22 (0.7, 2.15)	-
Pay attention to the traffic light guide to food (Often) (Reference: Always)	1.02 (0.78, 1.33)	-	1.06 (0.93, 1.2)	-	0.96 (0.67, 1.38)	-
Pay attention to the traffic light guide to food (Sometimes)	1.49 (0.78, 2.83)	-	0.76 (0.54, 1.06)	-	0.9 (0.35, 2.32)	-
Pay attention to the traffic light guide to food (Rarely)	1.12 (0.59, 2.15)	-	1.25 (0.99, 1.58)	-	0.71 (0.31, 1.63)	-
Pay attention to the traffic light guide to food (Never)	1.1 (0.48, 2.55)	-	0.77 (0.51, 1.18)	-	0.49 (0.17, 1.46)	-
Frequency of adding salt while eating (Often) (Reference: Always)	1.19 (0.76, 1.87)	-	0.95 (0.79, 1.13)	-	0.87 (0.51, 1.47)	-
Frequency of adding salt while eating (Sometimes)	1.1 (0.64, 1.87)	-	0.9 (0.66, 1.21)	-	1.03 (0.48, 2.21)	-
Frequency of adding salt while eating (Rarely)	0.99 (0.63, 1.57)	-	1.07 (0.84, 1.35)	-	1.01 (0.53, 1.93)	-
Frequency of adding salt while eating (Never)	0.98 (0.62, 1.54)	-	0.95 (0.75, 1.19)	-	1.01 (0.54, 1.89)	-
Frequency of eating salty foods Often) (Reference: Always)	0.89 (0.58, 1.35)	1.07 (0.69, 1.65)	1.03 (0.83, 1.27)	0.97 (0.8, 1.17)	0.96 (0.53, 1.75)	-
Frequency of eating salty foods (Sometimes)	0.46 (0.25, 0.84)	0.55 (0.28, 1.1)	1.24 (0.86, 1.79)	1.17 (0.83, 1.66)	0.38 (0.17, 0.88)	-
Frequency of eating salty foods (Rarely)	0.65 (0.42, 1.01)	0.7 (0.42, 1.18)	1.02 (0.74, 1.39)	0.94 (0.72, 1.23)	0.61 (0.36, 1.05)	-
Frequency of eating salty foods (Rarely)	0.51 (0.33, 0.8)	0.56 (0.34, 0.91)	1 (0.73, 1.36)	0.93 (0.72, 1.21)	0.35 (0.2, 0.63)	-

Table 4 (continued)

Variable	PR (95% CI) Crude	Adjusted PR (95% CI)	PR (95% CI) Crude	Adjusted PR (95% CI	PR (95% CI) Crude	Adjusted PR (95% CI)
Importance of salt reduction (Slightly important) (Reference: Very important)	0.38 (0.25, 0.59)	0.39 (0.24, 0.65)	1.04 (0.76, 1.41)	-	0.36 (0.21, 0.61)	0.35 (0.19, 0.65)
Importance of salt reduction (Not Important)	1.33 (1.04, 1.71)	1.18 (0.9, 1.55)	1.04 (0.91, 1.18)	-	1.46 (1.05, 2.02)	1.47 (1.03, 2.08)
Doctor's advice\ usage fruits or vegetables daily	1.16 (0.69, 1.93)	-	0.94 (0.71, 1.24)	-	0.88 (0.45, 1.72)	-
Doctor's advice\ decrease oil	1 (0.72, 1.39)	-	1.05 (0.9, 1.22)	-	0.97 (0.62, 1.5)	-
Doctor's advice\ do exercise	1.05 (0.74, 1.48)	-	1.07 (0.92, 1.26)	-	1.21 (0.73, 2)	-
Doctor's advice\ lose weight	1.01 (0.74, 1.37)	-	1.16 (1, 1.34)	-	0.93 (0.61, 1.42)	-

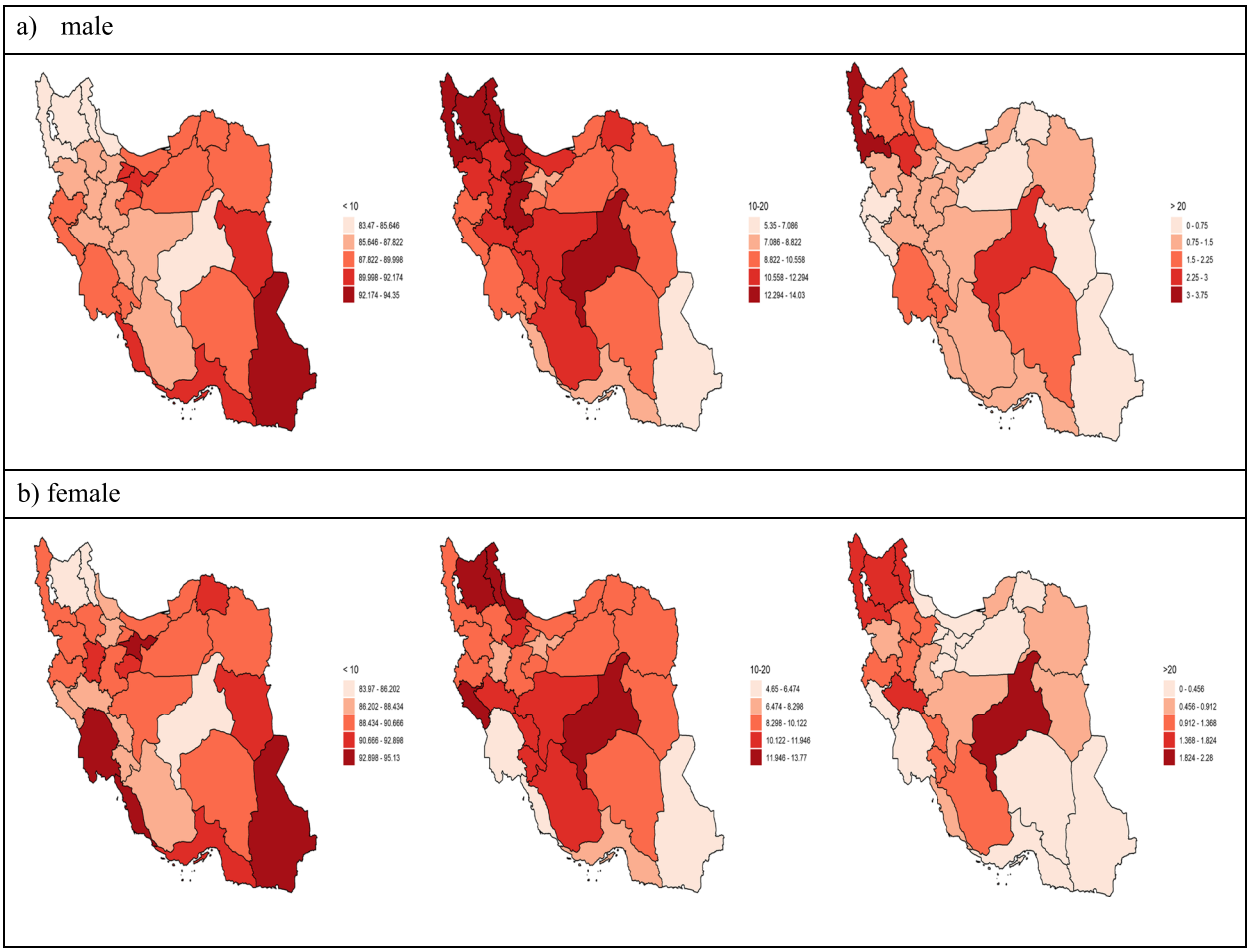

Fig. 2 The geographical distribution of adult patients with hypercholesterolemia according to the Framingham risk score (low (< 10%), intermediate (10%–20%), or high CVD risk (> 20%)

This could also highlight the differences in risk estimates when using the Framingham Risk Score across various socioeconomic or ethnic groups [27, 28].

Analysis of the components of the care cascade as a comprehensive view of the healthcare system's performance could be used for better planning and promotion of services [29]. Previous evidence confirmed that the effectiveness of hypercholesterolemia medications is directly linked to how consistently patients follow the prescribed therapeutic regimen. Among treated patients, the consistency in following the therapeutic regimen often declines to less than 60% after one year [11]. Many factors, such as a history of hospitalization, patients' underlying conditions, and the type of drug evaluation protocols, are linked to how consistently patients follow the therapeutic regimen and continue with LDL-lowering treatments [11–13].

Cholesterol management varies across other geographical regions. In US adults the target population for LDL-lowering medication estimated as 43.2 million (37.5%). In some conditions lipid monitoring reported in 88% of urban academic medical center of United State [30]. In Egypt, 37% of the population has elevated blood cholesterol levels, yet the overall target achievement for managing dyslipidemia is only 34.4% [31]. Similarly, in Turkey, just 26.2% of patients reached their target LDL-C levels [32]. These figures highlight the global challenge of effectively managing cholesterol, with disparities in treatment success and target achievement, particularly in middle- and low-income countries where non-HDL-C levels have increased over the past four decades [33].

In our study, the medication of hypercholesterolemia in urban areas was higher than in rural areas, which is in line with many studies could be attributed to on differences in socioeconomic status, heath literacy and even lifestyles patterns [11]. Related evidence showed that effective medication of hypercholesterolemia is not usually achieved in elderly populations, black or African-Americans, and those insured by Medicaid. Socioeconomic status and ethnic disparities in hypercholesterolemia treatment and control, are potentially rooted in difference levels of healthcare availability, seeking the services and access to care [30].

The association of preventive statin use and controlled levels of LDL were comparable to that reported through other epidemiological studies of hypercholesterolemia patients' [30, 34]. In some conditions, even in high-risk patients with the history of hospitalization for MI or undergoing elective coronary revascularization coverage of treatment estimated less than 50% [30].

Considering the second treatment guidelines which is estimated often based on CVD risk scores, the geographical patterns of distribution of high CVD risk patients (> 20%) was mostly concentrated in the northwestern provinces. Such a pattern is consistent with the higher prevalence of metabolic and lifestyle risk factors in these regions. At the top of these factors, we can point to the report of higher prevalence of obesity and overweight, unhealthy food patterns and inappropriate physical activity in previous studies. Along with these predisposing factors, the lowest risk (< 10%) was seen in the southeastern region and specifically in the Sistan and Baluchistan province [19, 35, 36].

The main implications of this study extend beyond identifying optimal treatment protocols. By thoroughly evaluating the prognostic roles of predisposing factors in lipid-modifying treatment regimens, we can refine and promote treatment guidelines, enhance patient compliance, and improve assessment methods [37]. These findings underscore a critical public health concern: the high prevalence of dyslipidemia in Iran remains largely unchanged despite previous governmental efforts, including regulation of dietary fats, public awareness campaigns, widespread statin prescription programs, and national action plans targeting non-communicable diseases.

This situation necessitates more effective and comprehensive health policies targeting the underlying risk factors contributing to dyslipidemia, such as obesity, physical inactivity, and unhealthy dietary habits. Urgent interventions are needed to curb the rising trend of obesity by promoting healthy eating habits—specifically, reducing the consumption of high-carbohydrate and refined-grain foods—and encouraging physical activity through culturally sensitive programs [11]. Additionally, improving public awareness and strengthening primary healthcare services are essential to enhance early detection and management of dyslipidemia. Implementing region-specific policies and adopting WHO-recommended interventions can considerably reduce the burden of dyslipidemia and help achieve national health objectives [13].

These findings should be interpreted in the context of the study's limitations. Firstly, its cross-sectional design poses challenges in identifying potential reverse associations between TC and assessed outcomes, as well as in establishing causality. We also have faced with some limitation in data availability about CHD (clinical CHD, symptomatic carotid artery disease, peripheral arterial disease, and abdominal aortic aneurysm) which we tried to replace with the underlying diabetes instead of CHD as CHD risk equivalent. As another consideration for the history of hypothyroidism and liver disorders, as the confounding factors for hypercholesterolemia, and adverse effects of drugs data was not collected in the survey study. Finally, the Framingham Risk Score included in

the NCEP ATP III guideline estimates the risk for hard CHD. However, due to the exclusion of individuals under 25 years of age in the final phase of the study, which included laboratory values for lipid profiles, there is a potential for overestimation of the hard CHD risk for the population. Additionally, the NCEP ATP III guideline's Framingham Risk Score for hard CHD is designed for populations under 80 years of age. Therefore, individuals older than 80 were excluded, necessitating caution when comparing the Framingham CHD Risk Score equivalents. While more recent guidelines—such as the 2013 ACC/AHA Guideline, the 2018 AHA/ACC/Multisociety Guideline on the Management of Blood Cholesterol, and other country-specific recommendations—have become prevalent globally, the NCEP ATP III guidelines remain widely utilized in the Iranian healthcare context for several reasons [18, 38, 39]. First, national healthcare infrastructure and clinical training programs are largely anchored to NCEP ATP III, making it the most pragmatic choice for a national-level study [40]. The existing screening, diagnostic, and treatment protocols for hypercholesterolemia in Iran are primarily based on these guidelines, allowing for comparability with past national surveys and consistency in longitudinal monitoring of hypercholesterolemia trends [41]. Additionally, there was some attrition between steps two (treatment eligibility assessment) and three (treatment initiation), which may introduce systematic bias if individuals who dropped out differed meaningfully from those who remained. For example, higher-risk participants might have been more motivated to continue, whereas healthier or less symptomatic individuals could have left the study. Such attrition could lead to either an overestimation or underestimation of treatment coverage, highlighting the need for caution when generalizing these results. Furthermore, we acknowledge the potential for a Healthy Participant Effect, wherein individuals who completed the entire study may be systematically healthier or more motivated to seek care than the general population. This bias could inflate treatment coverage estimates or adherence rates, as participants with a greater health awareness are more likely to participate in follow-up assessments, use preventive care, and respond to health surveys.

Nonetheless, it is important to acknowledge the limitations of using NCEP ATP III guidelines, as they have been superseded by more recent recommendations. Notably, newer guidelines often employ updated cardiovascular risk calculators (e.g., the Pooled Cohort Equations in ACC/AHA guidelines) and expanded evidence on statin therapy for primary prevention, which may lead to differing thresholds for initiating treatment. These updated guidelines also place a greater emphasis on patient-centered decision-making, lifestyle modification, and individualized risk factors—advancements that could better reflect the current evidence base [38, 39]. Furthermore, population heterogeneity in genetics, diet, and lifestyle might require adaptations or recalibrations of global guidelines to fit the Iranian context, potentially limiting the applicability of both NCEP ATP III and newer guidelines without local validation.

Ultimately, adopting more current guidelines in Iran would require substantial health policy revisions, resource allocation, and retraining of healthcare providers. Although this survey draws upon the NCEP ATP III framework for pragmatic and consistency reasons, there is a clear need for future studies to evaluate how newer global guidelines can be effectively adapted, validated, and integrated into the Iranian healthcare system.

Conclusion

In this population-based study, we quantified the national and sub-national diagnosis, coverage, and effectiveness of hypercholesterolemia pharmacotherapy in Iran, in accordance with the NCEP-ATP III guidelines. Our findings indicate that, although hypercholesterolemia prevalence is high, only about one-fifth of eligible individuals receive medication, with notable sex- and age-related disparities: coverage is higher among older adults and females. Statins dominate the therapeutic landscape but are underutilized, leaving large segments of at-risk populations—especially males, younger groups, and certain regions—without adequate care. Furthermore, the 10-year CHD risk in many individuals with hypercholesterolemia remains alarmingly high, emphasizing the urgency of more comprehensive strategies.

These results underscore the pressing need for enhanced screening and diagnosis, as well as robust coverage of evidence-based treatments to curtail hypercholesterolemia-related morbidity and mortality. Strengthening health system capacity, targeting high-risk subpopulations, and intensifying lifestyle interventions are priorities. Ultimately, bridging this treatment gap would not only improve lipid profiles at scale but also mitigate future cardiovascular burdens in Iran and other similar low- and middle-income settings.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12944-025-02506-9.

Supplementary Material 1.

Acknowledgements

This study was supported by the National Institute of Health Research of the Islamic Republic of Iran, affiliated with Tehran University of Medical Sciences, under Contract No. 241/M/9839. We extend our gratitude to all colleagues at

the Non-Communicable Diseases Research Center (NCDRC) and the Endocrinology and Metabolism Research Institute (EMRI) of Tehran University of Medical Sciences for their invaluable support.

Authors' contributions
All authors accepted the final version of the comment for publication. S.D. Idea Conceptualization & Writing Manuscript S.K. Revising Manuscript & Statistical Analysis MY. Statistical Analysis Supervision SS. Writing Manuscript ZSV: Revising Manuscript A.G. Revising Manuscript & Study Design & Statistical Analysis N.R. (Nazila Rezaei) Idea Conceptualization & Study Design AK. Laboratory Sample Collection and Processing ADM. Laboratory Sample Collection and Processing N.R. (Negar Rezaei) Idea Conceptualization & Study Design E.G. Idea Conceptualization, Study Design, Statistical Supervision N.A. Idea Conceptualization, Study Design, Statistical Supervision MMR. Idea Conceptualization, Study Design Y.F. Idea Conceptualization & Study Design & Project Manager K.R. Laboratory Sample Collection and Processing M.N. Laboratory Sample Collection and Processing S.A. Revising Manuscript & Study Design E.A. Laboratory Sample Collection and Processing R.H. Project Manager & Idea Conceptualization A.A.D. Laboratory Sample Collection and Processing A.M.R. Revising Manuscript & Study Design F.F. Revising Manuscript, Idea Conceptualization, Study Supervisor.

Funding
This study was funded by Endocrine & Metabolism Research Institute at Tehran University of Medical Sciences, Iran. Contract No. 1402–01-477–64018.

Data availability
All data generated and analyzed during this study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate
The research protocol for the study was approved by the Research Ethics Committees of the Endocrine & Metabolism Research Institute at Tehran University of Medical Sciences, with the approval number IR.TUMS.EMRI.REC.1402.017.

Competing interests
The authors declare no competing interests.

Author details
[1]Non-Communicable Diseases Research Center, Endocrinology and Metabolism Population Sciences Institute, Tehran University of Medical Sciences, Second Floor, No.10, Jalal Al-E-Ahmad Highway, Tehran 1411713137, Iran. [2]Development of Research and Technology Center, Deputy of Research and Technology Ministry of Health and Medical Education, Tehran, Iran. [3]Department of Mathematics and Statistics, Memorial University of Newfoundland, St. John's, NL, Canada. [4]Cell Science Research Center, Department of Stem Cells and Developmental Biology, Royan Institute for Stem Cell Biology and Technology, ACECR, Tehran, Iran. [5]Endocrinology and Metabolism Research Center, Endocrinology and Metabolism Clinical Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran. [6]Faculty of Medicine, Center for Life Course Health Research, University of Oulu, Oulu, Finland. [7]Heidelberg Institute of Global Health, Heidelberg University, Heidelberg, Germany.

Received: 29 November 2024 Accepted: 26 February 2025
Published online: 18 March 2025

References

1. Global burden of 288 causes of death and life expectancy decomposition in 204 countries and territories and 811 subnational locations, 1990–2021: a systematic analysis for the Global Burden of Disease Study 2021. Lancet. May 18 2024;403(10440):2100–2132. https://doi.org/10.1016/s0140-6736(24)00367-2
2. Fatollahzade M, Bastan M-M, Shaabanian M, et al. Sex disparity in the burden of NCDs and its four main subgroups in Iran 1990–2019: a systematic analysis from the global burden of disease study 2019. J Diab Metab Disord. 2024/09/09 2024. https://doi.org/10.1007/s40200-024-01489-1
3. UN. Sustainable development goals. 2030. Available at: https://sustainabledevelopment.un.org/?menu513002017.
4. Burden of cardiovascular diseases in the Eastern Mediterranean Region, 1990–2015: findings from the Global Burden of Disease 2015 study. Int J Public Health. 2018;63(Suppl 1):137–149. https://doi.org/10.1007/s00038-017-1012-3
5. Aryan Z, Mahmoudi N, Sheidaei A, et al. The prevalence, awareness, and treatment of lipid abnormalities in Iranian adults: Surveillance of risk factors of noncommunicable diseases in Iran 2016. J Clin Lipidol. 2018;12(6):1471-1481.e4. https://doi.org/10.1016/j.jacl.2018.08.001.
6. Grundy SM, Cleeman JI, Bairey Merz CN, et al. Implications of recent clinical trials for the national cholesterol education program adult treatment panel III guidelines. J Am Coll Cardiol. 2004;44(3):720–32.
7. Pencina MJ, Navar-Boggan AM, D'Agostino RB, et al. Application of new cholesterol guidelines to a population-based sample. N Engl J Med. 2014/04/10 2014;370(15):1422–1431. https://doi.org/10.1056/NEJMoa1315665
8. Pearson TA, Laurora I, Chu H, Kafonek S. The lipid treatment assessment project (L-TAP): a multicenter survey to evaluate the percentages of dyslipidemic patients receiving lipid-lowering therapy and achieving low-density lipoprotein cholesterol goals. Arch Intern Med. 2000;160(4):459–67. https://doi.org/10.1001/archinte.160.4.459.
9. Frolkis JP, Pearce GL, Nambi V, Minor S, Sprecher DL. Statins do not meet expectations for lowering low-density lipoprotein cholesterol levels when used in clinical practice. Am J Med. 2002;113(8):625–9.
10. Jafari A, Mirbehbahani SH, Golestani A, et al. Cardiometabolic risk factors trend in Iranian adults with hypertension over 15 years: findings of nationwide steps of 2007–2021. J Diab Metab Disord. 2024/09/23 2024. https://doi.org/10.1007/s40200-024-01498-0
11. Marcus ME, Ebert C, Geldsetzer P, et al. Unmet need for hypercholesterolemia care in 35 low- and middle-income countries: A cross-sectional study of nationally representative surveys. PLoS Med. 2021;18(10):e1003841. https://doi.org/10.1371/journal.pmed.1003841.
12. Khanali J, Ghasemi E, Rashidi M-M, et al. Prevalence of plasma lipid abnormalities and associated risk factors among Iranian adults based on the findings from STEPs survey 2021. Scient Rep. 2023/09/19 2023;13(1):15499. https://doi.org/10.1038/s41598-023-42341-5
13. Ochmann S, von Polenz I, Marcus ME, et al. Diagnostic testing for hypertension, diabetes, and hypercholesterolaemia in low-income and middle-income countries: a cross-sectional study of data for 994 185 individuals from 57 nationally representative surveys. Lancet Glob Health. 2023;11(9):e1363–71. https://doi.org/10.1016/s2214-109x(23)00280-2.
14. Djalalinia S, Azadnajafabad S, Ghasemi E, et al. Protocol Design for Surveillance of Risk Factors of Non–communicable Diseases During the COVID-19 Pandemic: An Experience from Iran STEPS Survey 2021. Arch Iran Med. 2022/9/1 2022;25(9):634–646. https://doi.org/10.34172/aim.2022.99
15. World Health Organization. The WHO STEPwise approach to noncommunicable disease risk factor surveillance (STEPS), WHO STEPS Instrument (Core and Expanded). Geneva: World Health Organization; 2015.
16. Worldwide trends in hypertension prevalence and progress in treatment and control from 1990 to 2019: a pooled analysis of 1201 population-representative studies with 104 million participants. Lancet. 2021;398(10304):957–980. https://doi.org/10.1016/s0140-6736(21)01330-1
17. Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. Circulation. 2002;106:3143–421. https://pubmed.ncbi.nlm.nih.gov/12485966/.
18. Executive Summary of The Third Report of The National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, And Treatment of High Blood Cholesterol In Adults (Adult Treatment Panel III). Jama. 2001;285(19):2486–97. https://doi.org/10.1001/jama.285.19.2486
19. Nejadghaderi SA, Ahmadi N, Rashidi M-M, Ghanbari A, Noori M, Abbasi-Kangevari M, Nasserinejad M, Rezaei N,Yoosefi M, Fattahi N: Physical activity pattern in Iran: Findings from STEPS 2021. Frontiers in Public Health 2022:10.
20. Organization WH. WHO STEPS Surveillance Manual. Geneva, Switzerland: World Health Organization; 2017.

21. Lumley, Thomas 2023 survey: Analysis of Complex Survey Samples R package (https://cran.r-project.org/package=survey) Research Resource Identifier (RRID): SCR_0128354.2–1.
22. RStudio Team 2023 RStudio: Integrated Development Environment for R RStudio, PBC Boston, MA http://www.rstudio.com Research Resource Identifier (RRID): SCR_000432.
23. R Core Team 2023 R: A Language and Environment for Statistical Computing R Foundation for Statistical Computing Vienna, Austria https://www.R-project.org Research Resource Identifier (RRID): SCR_001905.
24. caret: Classification And REgression Training. R package version 7.0.1. Available from https://CRAN.R-project.org/package=caret. RRID:SCR_021138.
25. Abbasi-Kangavari M, Masinaei M, Fattahi N, et al. Current inequities in smoking prevalence on district level in Iran: a systematic analysis on the STEPS survey. J Res Health Sci. 2021;22(1):e00540. https://doi.org/10.34172/jrhs.2022.75
26. MB AA, WA K. Cardiovascular diseases risk prediction using the Framingham risk score. Egypt J Occup Med. 2021;45(3):249–264. https://doi.org/10.21608/ejom.2021.193283
27. D'Agostino RB, Sr, Grundy S, Sullivan LM, Wilson P, Group ftCRP. Validation of the Framingham coronary heart disease prediction scores: results of a multiple ethnic groups investigation. JAMA. 2001;286(2):180–187. https://doi.org/10.1001/jama.286.2.180
28. Brindle PM, McConnachie A, Upton MN, Hart CL, Davey Smith G, Watt GC. The accuracy of the Framingham risk-score in different socioeconomic groups: a prospective study. Br J Gen Pract. 2005;55(520):838–45.
29. Tran C, Vo V, Taylor P, Koehn DA, Virani SS, Dixon DL. Adherence to lipid monitoring and its impact on treat intensification of LDL-C lowering therapies at an urban academic medical center. J Clin Lipidol. 2022;16(4):491–7.
30. Zheutlin AR, Derington CG, Herrick JS, et al. Lipid-Lowering Therapy Use and Intensification Among United States Veterans Following Myocardial Infarction or Coronary Revascularization Between 2015 and 2019. Circ Cardiovasc Qual Outcomes. 2022;15(12): e008861. https://doi.org/10.1161/circoutcomes.121.008861.
31. Taha H, Badran HM, Kandil H, et al. Egyptian practical guidance in lipid management 2020. Egypt Heart J. 2021;73(1):17. https://doi.org/10.1186/s43044-021-00140-1.
32. Şen T, Dinç Asarcıklı L, Güven S, et al. Adherence to current dyslipidemia guideline in patients utilizing statins according to risk groups and gender differences: The AIZANOI Study. Anatol J Cardiol. 2024;28(6):273–282. https://doi.org/10.14744/AnatolJCardiol.2024.4218
33. Pirillo A, Norata GD. The burden of hypercholesterolemia and ischemic heart disease in an ageing world. Pharmacol Res. 2023/07/01/ 2023;193:106814. https://doi.org/10.1016/j.phrs.2023.106814
34. Foley TR, Singh GD, Kokkinidis DG, Choy HK, Pham T, Amsterdam EA, Rutledge JC, Waldo SW, Armstrong EJ, Laird JR: High-Intensity Statin Therapy Is Associated With Improved Survival in Patients With Peripheral Artery Disease. J Am Heart Assoc 2017:6.
35. Djalalinia S, Saeedi Moghaddam S, Sheidaei A, Rezaei N, Naghibi Iravani SS, Modirian M, Zokaei H, Yoosefi M, Gohari K, Kousha A, et al: Patterns of Obesity and Overweight in the Iranian Population: Findings of STEPs 2016. Front Endocrinol (Lausanne). 2020;11:42.
36. Djalalinia S, Yoosefi M, Shahin S, et al. The levels of BMI and patterns of obesity and overweight during the COVID-19 pandemic: Experience from the Iran STEPs 2021 survey. Front Endocrinol. 2022;13:1043894.
37. Behnoush AH, Khosravi S, Ziamanesh F, et al. Blood Pressure Control Among Diabetic Patients in the Eastern Mediterranean Region: A Systematic Review and Meta-Analysis. Curr Diabetes Rev. 2024. https://doi.org/10.2174/0115733998327293240729080250.
38. Stone NJ, Robinson JG, Lichtenstein AH, et al. 2013 ACC/AHA guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol. 2014;63(25 Pt B):2889–934. https://doi.org/10.1016/j.jacc.2013.11.002
39. Grundy SM, Stone NJ, Bailey AL, et al. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol: Executive Summary: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol. 2019;73(24):3168–209. https://doi.org/10.1016/j.jacc.2018.11.002.
40. Yousefi M, Dastan I, Alinezhad F, et al. Prevention and control of noncommunicable diseases in iran: the case for Investment. BMC Public Health. 2022;22(1):1248. https://doi.org/10.1186/s12889-022-13615-w.
41. Peykari N, Hashemi H, Dinarvand R, et al. National action plan for noncommunicable diseases prevention and control in Iran; a response to emerging epidemic. J Diabetes Metab Disord. 2017;16:3. https://doi.org/10.1186/s40200-017-0288-4.

Publisher's Note