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Incidence and risk factors for cardiovascular mortality in Iranian adults: Findings from a 10-year Yazd Healthy Heart Project Study

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Abstract

BACKGROUND: Cardiovascular disease (CVD) is the leading cause of death worldwide, with a growing burden in low- and middle-income countries. Given the increasing CVD mortality in Iran and the limited evidence on long-term lifestyle determinants, a cohort study is needed to examine the effects of related factors.

METHODS: A total of 2,000 adults, including 1,000 men and women aged 20 to 74 years, were enrolled in a population-based cohort study in Yazd, Iran, from 2005 to 2006, with a mean follow-up of 10 years. Cox proportional hazards models were used to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) for CVD mortality in relation to demographic, economic status, educational, and lifestyle factors.

RESULTS: During follow-up, 83 CVD deaths occurred (5.4%). The mortality rate was 6.8% in men and 3.8% in women. After adjustment for hypertension, diabetes, and hypercholesterolemia, significant predictors of CVD mortality included age ≥65 years (HR = 3.63, 95% CI: 2.28-5.77), male sex (HR = 2.29, 95% CI: 1.31-3.34), and smoking (HR = 1.95, 95% CI: 1.21-3.13). In contrast, moderate physical activity was associated with a lower risk of mortality (HR = 0.38, 95% CI: 0.17-0.84), and high school education was also protective (HR = 0.49, 95% CI: 0.25-0.98). In subgroup analyses among men, age ≥65 years, moderate physical activity, and high school education remained significant predictors of CVD mortality ($P < 0.05$).

CONCLUSION: Age 65 years or older, smoking, and male sex increased the risk of CVD mortality in this Iranian cohort. Physical activity and higher educational attainment were associated with a reduced risk of CVD mortality.

Keywords: Cardiovascular Disease, Mortality; Risk Factors; Incidence; Cohort Studies

Introduction

Cardiovascular disease (CVD) represents a significant challenge to global public health, with an estimated 523 million individuals living with various forms of the disease[1,2]. Annually, approximately 19 million deaths are attributed to cardiovascular-related causes, accounting for nearly one-third of all global mortality[1]. Between 1990 and 2019, the global number of deaths from CVD rose significantly, from 12.1 million to 18.6 million[2]. In 2019, the death rate from CVD in Iran was 46%, highlighting the urgent need to identify high-risk groups for targeted public health interventions[3].

While hypertension, dyslipidemia, obesity, and diabetes are well-known risk factors for CVD morbidity and mortality[4], emerging evidence highlights the significant role of sociodemographic and behavioral factors as well[5-8]. A Finnish cohort study by Mikkola et al. highlights that mortality rates from CVD increase with age, and men face an 80% higher risk than women, with rates of 442 and 246 per 100,000, respectively[5]. Furthermore, individuals with lower incomes or educational attainment experience heightened risks[6,9]. a 17-year study found that those with low socioeconomic status are approximately 80% more likely to die from heart-related conditions[6]. Smoking exacerbates this risk, with hazard ratios of 2.58 for men and 3.79 for women compared to non-smokers[7]. Conversely, physical activity provides protective benefits against CVD[8]. These findings underscore the necessity for context-specific research given the variability of these relationships across different populations.

CVD mortality is notably high in low- and middle-income nations, such as Iran, where it stands as one of the most important causes of death[3]. As CVD mortality imposes a considerable financial burden on the healthcare system and negatively affects overall health, it is essential to investigate the risk factors associated with CVD mortality[10]. Previous studies in Iran and other Middle Eastern countries have investigated the effects of age, gender, economic status, physical activity and smoking on CVD mortality[11,12]. Our research is the first in Central Iran to examine these risk factors over a 10-year follow-up period within the Yazd Healthy Heart Cohort. This extended study period provided valuable insights to develop effective prevention strategies in Middle Eastern countries. Additionally, our gender-stratified analysis stands out as a key contribution of this research.

Material and Method

Study population

This research was conducted using data from the Yazd Health and Heart Project (YHHP) in Yazd, Iran. In the initial phase, a cohort of 2,000 individuals, including 1,000 men and 1,000 women aged 20 to 74 years, was randomly selected between 2005 and 2006. After a nearly 10-year follow-up, eligible participants were invited to take part in the second phase of the study.

The main follow-up examination for biochemical and clinical measures was conducted during the second phase, between 2015 and 2016. However, the primary outcome, CVD mortality, and vital status were ascertained through continuous prospective surveillance. This approach allowed precise determination of each participant's follow-up time, defined as the interval from the date of the baseline examination to the date of CVD mortality, non-CVD mortality, or the last confirmed vital status. Consequently, individual follow-up duration varied, ranging from approximately 9 to 11 years.

Diagnosis of fatal cardiovascular events

Data on fatal cardiovascular events were obtained through telephone follow-up with next of kin, supplemented by a review of available medical and hospital records when accessible. Predicted fatal CVD was obtained using the Framingham general CVD risk score[13,14]. Fatal cardiovascular events encompass a range of conditions leading to mortality, including peripheral artery disease, Coronary heart disease, strokes, heart failure, and fatal myocardial infarction (MI). These events also include deaths that occur after interventional procedures like percutaneous coronary intervention (PCI) and coronary artery bypass grafting (CABG)[13].

Additionally, the diagnosis of new cases of angina is carried out using the Rose angina questionnaire, which is validated by corroborative data from electrocardiograms, elevated levels of cardiac enzymes, a positive exercise tolerance test, or results from a coronary angiogram[14]. All fatalities attributed to CVD are considered in the overall assessment of fatal cardiovascular events.

Exposure variables

Demographic variables, including gender and age, were collected at baseline through a specific data collection form conducted by trained interviewers in the first phase.

Also, other variables, including educational level, economic status, physical activity, and smoking habits, were evaluated using forms. The educational levels are distinctly classified as primary, high school, or academic. The economic status of the participants was determined by examining their household income, private car ownership, and home size (square meters). Participants were categorized into low, moderate, or high economic status based on their total score after evaluating each item. Physical activity levels were evaluated using the International Physical Activity Questionnaire (IPAQ)[15], which categorizes individuals into three groups based on their weekly caloric expenditure: low activity (less than 600 kcal), moderate activity (600 to 1200 kcal), and vigorous activity (more than 1200 kcal). Participants were further classified by smoking status as either current smokers or non-smokers. The non-smoker category included both individuals who had never smoked and those who had ceased smoking before the baseline assessment.

Other variables

Blood pressure measurements were taken twice using a digital monitor (M6 Comfort from Omron Co., Osaka, Japan) after a 5-minute resting period, with additional measurements recorded at 5-minute intervals. For the purposes of analysis, average values for systolic and diastolic blood pressure were utilized. Hypertension was characterized by systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg or the use of medications for hypertension[16,17].

Morning blood samples were collected after an overnight fast. All bioassays were performed in a single laboratory, utilizing a biochemical autoanalyzer (BT 3000, Italy). Lipid profiles, which included total cholesterol (TC), low-density lipoprotein (LDL), and high-density lipoprotein (HDL), were evaluated using Bionic kits (Bionic Company, Tehran, Iran), while triglycerides (TG) and fasting blood sugar (FBS) were measured with a diagnostic kit from Pars Azmoon Inc. (Tehran, Iran). According to previous studies, diabetes was defined by fasting glucose ≥126 mg/dl[18], while high cholesterol was defined by serum cholesterol ≥240 mg/dl[19].

Trained personnel collected anthropometric data using equipment and standardized methods. Height measurements were obtained while participants stood against a wall, ensuring that their heels, hips, shoulders, and heads were in contact with the surface and that their heads were aligned horizontally. The height was recorded to the nearest 0.5 cm. Weight measurements were recorded using digital scales (Seca, Germany) in the first phase of the study and a different scale (Omron BF511, Karada Body Scan, Osaka, Japan) in the second phase, both accurate to 0.1 kg. BMI (Body Mass Index) was determined by dividing weight (in kilograms) by height squared (in meters). Additionally, waist circumference was measured at the midpoint between the bottom of the last visible rib and the top of the iliac crest. Measurements of height, weight, and waist circumference were taken while participants were in minimal clothing and without shoes.

Statistical analysis

Continuous variables were presented as means with standard deviations (SD), whereas categorical variables were shown as percentages. Continuous variables were analyzed using

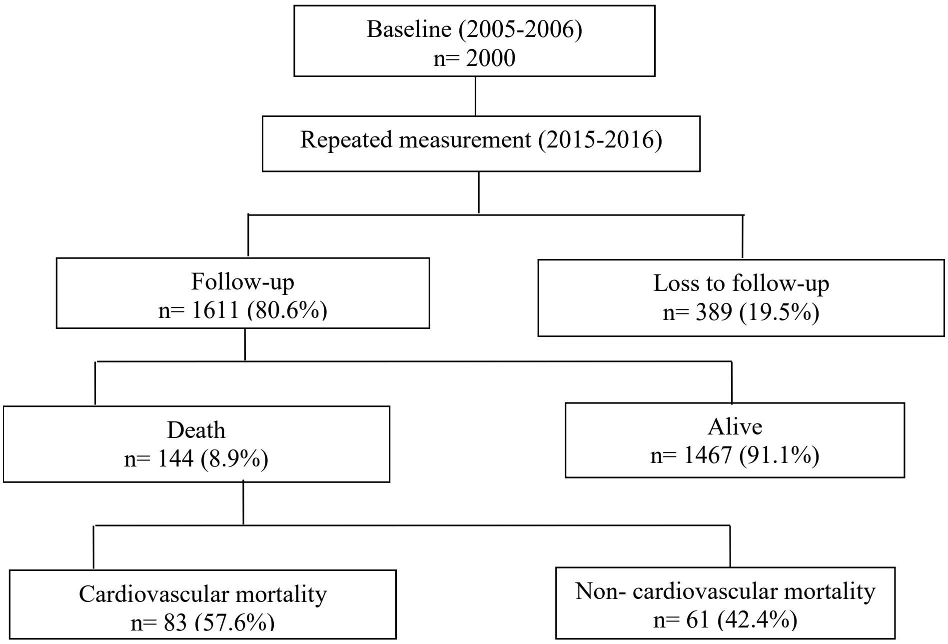

Figure 1. Flow diagram showing the recruiting process during approximately a 10-year follow-up study for cardiovascular mortality

independent t-tests, whereas categorical variables were assessed using chi-square tests. Cox proportional hazards models were used to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) for CVD mortality. A crude model and a multivariable-adjusted model were used, adjusting for factors such as hypertension, diabetes, and high cholesterol. Incidence rates were calculated as the number of events divided by the total person-time at risk for the relevant subgroup and expressed per 1,000 person-years. All analyses were performed using SPSS version 19 (IBM Corp., Armonk, NY, USA), with statistical significance established at $P < 0.05$.

Results

Characteristics of the sample

In the first phase of the prospective study, 2,000 participants were recruited (Figure 1). In the second phase, 1,611 participants were followed up and assessed. Among the participants, there were 144 fatalities (8.9%), including 83 deaths caused by CVD and 61 deaths due to non-cardiovascular causes. Ultimately, the baseline characteristics collected during 2005-2006 of participants who later died from CVD were compared with those of participants who survived the follow-up period. Significant differences were observed in age, weight, BMI, blood pressure, glucose levels, TG, cholesterol, LDL cholesterol, gender, smoking, economic status, physical activity, and education ($P < 0.05$) (Table 1).

CVD Mortality rates

The overall 10-year cumulative incidence of CVD mortality was 5.4% (83/1,550). The annual CVD mortality incidence rates were 0.69% for men, 0.38% for women, and 0.54% for the total cohort.

The CVD mortality risk over the nearly 10-year follow-up period is presented in Table 2. The incidence of CVD mortality among individuals aged 65 years and older was 15.14 per 1,000 person-years, markedly higher than that observed in younger participants. Moreover, CVD mortality rates were higher among men, smokers, individuals with high economic status, and those with only primary education compared with others.

Table 1. Characteristics of participants who died from cardiovascular disease and who remained alive after approximately a 10-year follow-up

Variable	Alive N= 1467	CVD mortality N= 83	P value
Age (year)	47.7±14.4	63.0±10.3	<0.001
Women (%)	716 (48.8)	28 (33.7)	0.007
Weight (Kg)	71.6±12.7	68.4±13.8	0.027
Body Mass Index (Kg/m²)	26.23±4.32	25.53±4.04	0.015
Systolic blood pressure (mmHg)	127±15	140±18	<0.001
Diastolic blood pressure (mmHg)	82±9	87±10	<0.001
Fasting blood sugar (mg/dL)	101.15±42.01	142.71±85.52	<0.001
Triglyceride (mg/dL)	175.91±108.33	206.2±117.03	0.014
Cholesterol (mg/dL)	198.29±44.18	216.78±51.1	<0.001
LDL (mg/dL)	108.39±36.22	118.8±39.65	0.012
HDL (mg/dL)	54.1±13.81	54.44±13.36	0.827
Waist circumference (cm)	93.74±12.01	95.9±12.28	0.113
Current smokers (%)	251 (17.1)	25 (30.1)	0.003
Physical activity (%)			
Low	662 (66.4)	54 (87.1)	
Moderate	287 (28.8)	7 (11.3)	0.003
Vigorous	48 (4.8)	1 (1.6)	
Economic Status (%)			
Low	188 (28.2)	17 (50)	
Moderate	269 (40.3)	6 (17.6)	0.009
High	210 (31.5)	11 (32.4)	
Education (%)			
Primary	828 (58.1)	67 (80.7)	
High school	455 (31.9)	10 (12)	<0.001
Academic	143 (10)	6 (7.2)	

Results are presented as percentages for categorical variables and as means ± standard deviations for continuous variables.

Table 2. Risk of cardiovascular mortality after approximately a 10-year follow-up

Variable		At risk (n)	Person year	Cases (n)	Incidence/1000 person-year	Hazard ratio (95%CI) Crude	Hazard ratio (95%CI) Adjusted model*
Age group							
	<65	1307	12916	37	2.86	1	1
	>65	304	3038	46	15.14	5.35 (3.47-8.24)	3.63 (2.28-5.77)
Gender	Woman	769	7635	28	3.67	1	1
	Men	842	8313	55	6.61	1.83 (1.16-2.89)	2.29 (1.31–3.34)
Smoking	Non-smoker	1314	12998	58	4.46	1	1
	Smoker	292	2906	25	8.6	1.85 (1.16-2.96)	1.95 (1.21-3.13)
Physical activity							
	Low	753	7478	54	7.22	1	1
	Moderate	300	2987	7	2.34	0.33 (0.15-0.72)	0.38 (0.17-0.84)
	Vigorous	51	514	1	1.94	0.23 (0.03-1.68)	0.28 (0.04-2.07)
Economic Status							
	Low	218	2207	17	7.7	1	1
	Moderate	282	2816	6	2.13	0.30 (0.12-0.75)	0.40 (0.16-2.04)
	High	223	2221	11	4.95	0.67 (0.31-1.43)	0.85 (0.39-1.83)
Education							
	primary	947	9391	76	8.09	1	1
	High school	470	4618	10	2.16	0.30 (0.16-0.59)	0.49 (0.25-0.98)
	Academic	153	1529	6	3.92	0.51 (0.22-1.17)	0.69 (0.30-1.60)

Results are reported as a hazard ratio with a 95% confidence interval.
*These results are adjusted for hypertension, diabetes, and high cholesterol.

Factors associated with CVD mortality

In the crude model, participants older than 65 years exhibited a significantly elevated risk of CVD mortality (HR = 5.35; 95% CI: 3.47-8.24) compared with those younger than 65 years. After adjustment, the association remained significant (HR = 3.63, 95% CI: 2.28-5.77). Furthermore, men showed a higher hazard than women in both the crude (HR = 1.83, 95% CI: 1.16-2.89) and adjusted models (HR = 2.29, 95% CI: 1.31-3.34).

Smoking was identified as a significant contributor to increased CVD mortality risk in both the crude (HR = 1.85, 95% CI: 1.16-2.96) and adjusted analyses (HR = 1.95, 95% CI: 1.21-3.13). Participation in moderate physical activity was associated with a reduced risk in the crude model (HR = 0.33, 95% CI: 0.15-0.72) and the adjusted model (HR = 0.38, 95% CI: 0.17-0.84).

Moderate economic status was associated with reduced CVD mortality in the crude model (HR = 0.30, 95% CI: 0.12-0.75), but this effect was no longer significant after adjustment (HR = 0.40, 95% CI: 0.16-2.04). High economic status showed no significant association in either model. For educational level, individuals with a high school education had a significantly lower CVD risk compared with those with only a primary education in both crude (HR = 0.30, 95% CI: 0.16-0.59) and adjusted models (HR = 0.49, 95% CI: 0.25-0.98).

The results stratified by gender are provided in Tables 3 and 4. In both genders, the risk of CVD mortality was significantly higher among participants aged 65 years or older in men (HR = 3.17; 95% CI: 1.82-5.54) and women (HR = 4.92; 95% CI: 2.10-11.60) in the adjusted model. Also, moderate physical activity (HR = 0.35; 95% CI: 0.14-0.89) and education (HR = 0.41; 95% CI: 0.20-0.86) were predictors of CVD mortality in men ($P < 0.05$).

Discussion

Previous studies indicate that age and gender-factors beyond our control-significantly contribute to the risk of mortality from CVD. Our findings align with this understanding. Specifically, we observed that participants aged 65 and older are at a greater risk of dying from CVD compared to those younger than 65, making age the strongest predictor of this outcome. The aging process contributes to

Table 3. Risk of cardiovascular mortality after approximately a 10-year follow-up in men

Variable		At risk (n)	Person year	Cases (n)	Incidence/1000 person-year	Hazard ratio (95%CI) Crude	Hazard ratio (95%CI) Adjusted model*
Age group							
	<65	686	6779.66	28	4.13	1	1
	>65	156	1539.8	27	17.53	4.55 (2.68-7.72)	3.17 (1.82-5.54)
Smoking	Non-smoker	554	5454.44	30	5.5	1	1
	Smoker	284	2825.5	25	8.85	1.51 (0.89-2.57)	1.51 (0.88-2.56)
Physical activity							
	Low	460	4524.49	39	8.62	1	1
	Moderate	168	1669.63	5	2.909	0.33 (0.13-0.84)	0.35 (0.14-0.89)
	Vigorous	39	391.98	1	2.55	0.25 (0.03-1.80)	0.28 (0.40-2.09)
Economic Status							
	Low	116	1157.88	14	12.1	1	1
	Moderate	187	1853.57	6	3.24	0.29 (0.11-0.75)	0.43 (0.16-1.15)
	High	142	1412	10	7.08	0.61 (0.27-1.38)	0.81 (0.35-1.83)
Education							
	Primary	401	3961.37	40	10.1	1	1
	High school	288	2829.47	9	3.18	0.30 (0.15-0.62)	0.41 (0.20-0.86)
	Academic	123	1228.63	6	4.88	0.41 (0.17-0.98)	0.50 (0.21-1.95)

Results are reported as a hazard ratio with a 95% confidence interval.
*These results are adjusted for hypertension, diabetes, and high cholesterol.

Table 4. Risk of cardiovascular mortality after approximately a 10-year follow-up in women

Variable		At risk (n)	Person year	Cases (n)	Incidence/1000 person-year	Hazard ratio (95%CI) Crude	Hazard ratio (95%CI) Adjusted model*
Age group							
	<65	621	6136.66	9	1.47	1	1
	>65	148	1498.36	19	12.68	8.31 (3.76-18.37)	4.92 (2.10-11.60)
Smoking	Non-smoker	760	7543.99	28	3.71	-	-
	Smoker	8	81.15	7	86.26	-	-
Physical activity							
	Low	293	2953.63	15	5.08	1	1
	Moderate	132	1318.82	2	1.52	0.32 (0.07-1.39)	0.46 (0.10-2.03)
	Vigorous	12	122.97	0	-	-	-
Economic Status							
	Low	102	1049.4	3	2.86	1	1
	Moderate	95	963.28	0	-	-	-
	High	81	809.22	1	1.23	0.43 (0.045-4.13)	0.70 (0.71-7.00)
Education							
	Primary	546	5430.15	27	5.96	1	1
	High school	182	1789.12	1	0.56	0.12 (0.016-0.85)	0.31 (0.04-2.37)
	Academic	30	300.68	0	-	-	-

Results are reported as a hazard ratio with a 95% confidence interval.
*These results are adjusted for hypertension, diabetes, and high cholesterol.

vascular alterations, such as arterial stiffening and endothelial dysfunction, which exacerbate atherosclerosis. Consequently, the incidence of fatal cardiovascular events increases markedly with age, with individuals over 65 accounting for over 80% of CVD deaths[20]. This burden is particularly pronounced in women, as the decline in estrogen levels associated with menopause around age 50 leads to a worsening of cardiovascular risk factors and heightened risk of CVD and mortality. Thus, menopause represents a critical period to implement preventive strategies aimed at reducing CVD risk in women[21]. In addition, in the research conducted by Talaei et al., it was observed that the incidence of death from cardiovascular events escalates exponentially with age, reaching a peak among individuals aged 65 to 74 years[22]. In our study, we found that individuals over the age of 65 exhibit an incidence rate of 17.53 deaths per 1,000 person-years, aligning with other research[20,22]. Furthermore, while a notable gender disparity in CVD mortality was reported, with men experiencing a rate of 331 per 100,000 person-years compared to 203 for women, this difference did not achieve statistical significance in their study[22]. Conversely, a recent study reported that a significant variation in CVD mortality rates between genders, with men being more likely to die from CVD, with an 80% higher risk compared to women, that are similar to our findings[5]. In addition, a significant gender gap in CVD mortality was shown in Lithuania and France, with men at a higher risk than women[23]. These findings underscore the need to consider age and gender when evaluating health outcomes, as well as the necessity for further research into gender disparities in health outcomes.

Extensive research conducted has consistently established a strong association between modifiable life factors-specifically smoking, physical inactivity, low socioeconomic status, and low educational attainment-and an increased risk of death from CVD[24–27]. Our analysis suggested that obtaining an education beyond the high school level may reduce the risk of CVD mortality, further supporting existing literature[9,28]. Conversely, our findings indicated that low economic status is not associated with higher mortality rates from CVD, contradicting earlier studies[24]. The association between economic status and CVD mortality is complex and may differ based on factors such as study design, the demographics of the population, measurement of economic status and the impact of confounding variables.

In addition to the mentioned factors, personal behaviors such as physical activity are crucial in mitigating CVD risk. A meta-analysis has indicated that leisure-time physical activity correlates negatively with CVD mortality risk across various demographics, although the protective effect is less pronounced in individuals over 65 or with a history of CVD[26]. Our study highlights a clear association between physical activity levels and CVD mortality rates: individuals engaging in moderate physical activity have the lowest mortality risk compared to those with low levels of physical activity. Our findings align with existing evidence demonstrating that moderate physical activity alone reduce substantial the risk of death from CVD[29]. Exercise-only training had been shown to significantly reduce pooled cardiac mortality by 28%[30]. Moderate physical activity appears to reduce CVD mortality, particularly among men. However, this positive association was not observed in women, which may suggest that the physical activity data for women in the study were not adequate for reaching firm conclusions.

Our findings showed that although smoking is a notable risk factor for CVD mortality, its association with CVD mortality does not achieve statistical significance when assessed by gender. This lack of significance may be attributed to the small number of smokers, particularly among women, which limited our statistical power and resulted in unstable estimates of the HR. A Study showed that a longer duration of smoking cessation reduced mortality risks, including CVD[27]. Notably, a study examining cigarette smoking's effect on the education-mortality gap among U.S. adults found that lower educational attainment was associated with higher mortality rates, primarily due to the higher prevalence and longer duration of smoking among individuals with less education, especially among men and younger women[31]. These results underscored the role of smoking as a key factor in mortality risk differences linked to education, highlighting the influence of age and gender in smoking behaviors[31].

Strengths and limitation

This study had several notable strengths. It represented the first long-term cohort analysis in Yazd, Iran, to examine lifestyle and sociodemographic factors related to CVD mortality, with a follow-up period of nearly a decade. Standardized data collection and validated measures improved the study's internal validity. In addition, the population-based sample provided region-specific insights into CVD risk factors in Middle Eastern populations, where data are limited.

There were several limitations to note. The modest sample size restricted subgroup analyses by gender and physical activity. In addition, the study did not account for confounding factors such as dietary habits, genetic predisposition, or clinical history. Because the study was conducted in a single geographic region, the findings may not be fully generalizable to populations with different cultural, environmental, or socioeconomic contexts. Moreover, because the data were collected from 2005 to 2015, the findings may not be directly applicable to today's populations, particularly given changes in lifestyle and healthcare.

Conclusion

This cohort analysis confirmed that older age and smoking increase the risk of CVD mortality, with men facing a higher risk than women. Conversely, moderate physical activity and high school education provided significant protective benefits. Interventions targeting these factors could substantially reduce the cardiovascular burden in similar middle-income populations.

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Conflict of interests

The authors declare no conflict of interest.

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Author's Contributions

Study Conception or Design: MS; SQ; MK; HM; SM

Data Acquisition: MS

Data Analysis or Interpretation: MS; SQ; LH; PMV; AS

Manuscript Drafting: MS; SQ; MK; HM

Critical Manuscript Revision: LH; PMV; AS; SM

All authors have approved the final manuscript and are responsible for all aspects of the work.

References

1. Coronado F, Melvin SC, Bell RA, Zhao G. Global Responses to Prevent, Manage, and Control Cardiovascular Diseases. Prev Chronic Dis. 2022 Dec 8;19:E84. https://doi.org/10.5888/pcd19.220347
2. Roth GA, Mensah GA, Johnson CO, Addolorato G, Ammirati E, Baddour LM, et al. Global Burden of Cardiovascular Diseases and Risk Factors, 1990-2019: Update From the GBD 2019 Study. J Am Coll Cardiol. 2020 Dec 22;76(25):2982-3021. https://doi.org/10.1016/j.jacc.2020.11.010
3. Sarrafzadegan N, Mohammmadifard N. Cardiovascular Disease in Iran in the Last 40 Years: Prevalence, Mortality, Morbidity, Challenges and Strategies for Cardiovascular Prevention. Arch Iran Med. 2019 Apr 1;22(4):204-10.
4. Vaduganathan M, Mensah GA, Turco JV, Fuster V, Roth GA. The Global Burden of Cardiovascular Diseases and Risk: A Compass for Future Health. J Am Coll Cardiol. 2022 Dec 20;80(25):2361-71. https://doi.org/10.1016/j.jacc.2022.11.005
5. Mikkola TS, Gissler M, Merikukka M, Tuomikoski P, Ylikorkala O. Sex differences in age-related cardiovascular mortality. PLoS One. 2013 May 20;8(5):e63347. https://doi.org/10.1371/journal.pone.0063347
6. Kamphuis CB, Turrell G, Giskes K, Mackenbach JP, van Lenthe FJ. Socioeconomic inequalities in cardiovascular mortality and the role of childhood socioeconomic conditions and adulthood risk factors: a prospective cohort study with 17-years of follow up. BMC Public Health. 2012 Dec 5;12:1045. https://doi.org/10.1186/1471-2458-12-1045
7. Vallée A. Associations between tobacco smoking and mortality: a sex-stratified cohort analysis. Eur J Public Health. 2025 Dec 1;35(6):1212-8. https://doi.org/10.1093/eurpub/ckaf194
8. Barengo NC, Hu G, Lakka TA, Pekkarinen H, Nissinen A, Tuomilehto J. Low physical activity as a predictor for total and cardiovascular disease mortality in middle-aged men and women in Finland. Eur Heart J. 2004 Dec;25(24):2204-11. https://doi.org/10.1016/j.ehj.2004.10.009
9. Khan N, Javed Z, Acquah I, Hagan K, Khan M, Valero-Elizondo J, et al. Low educational attainment is associated with higher all-cause and cardiovascular mortality in the United States adult population. BMC Public Health. 2023 May 16;23(1):900. https://doi.org/10.1186/s12889-023-15621-y
10. Rittiphairoj T, Bulstra C, Ruampatana C, Stavridou M, Grewal S, Reddy CL, et al. The economic burden of ischaemic heart diseases on health systems: a systematic review. BMJ Glob Health. 2025 Feb 12;10(2):e015043. https://doi.org/10.1136/bmjgh-2024-015043
11. Hadaegh F, Derakhshan A, Mozaffary A, Hasheminia M, Khalili D, Azizi F. Twelve-Year Cardiovascular and Mortality Risk in Relation to Smoking Habits in Type 2 Diabetic and Non-Diabetic Men: Tehran Lipid and Glucose Study. PLoS One. 2016 Mar 1;11(3):e0149780. https://doi.org/10.1371/journal.pone.0149780
12. Lear SA, Hu W, Rangarajan S, Gasevic D, Leong D, Iqbal R, et al. The effect of physical activity on mortality and cardiovascular disease in 130 000 people from 17 high-income, middle-income, and low-income countries: the PURE study. Lancet. 2017 Dec 16;390(10113):2643-54. https://doi.org/10.1016/S0140-6736(17)31634-3
13. Chia YC, Gray SY, Ching SM, Lim HM, Chinna K. Validation of the Framingham general cardiovascular risk score in a multiethnic Asian population: a retrospective cohort study. BMJ Open. 2015 May 19;5(5):e007324. https://doi.org/10.1136/bmjopen-2014-007324
14. Rahman MA, Spurrier N, Mahmood MA, Rahman M, Choudhury SR, Leeder S. Rose Angina Questionnaire: validation with cardiologists' diagnoses to detect coronary heart disease in Bangladesh. Indian Heart J.

2013 Jan-Feb;65(1):30-9. https://doi.org/10.1016/j.ihj.2012.09.008
15. Craig CL, Marshall AL, Sjöström M, Bauman AE, Booth ML, Ainsworth BE, et al. International physical activity questionnaire: 12-country reliability and validity. Med Sci Sports Exerc. 2003 Aug;35(8):1381-95. https://doi.org/10.1249/01.MSS.0000078924.61453.FB
16. Unger T, Borghi C, Charchar F, Khan NA, Poulter NR, Prabhakaran D, et al. 2020 International Society of Hypertension Global Hypertension Practice Guidelines. Hypertension. 2020 Jun;75(6):1334-57. https://doi.org/10.1161/HYPERTENSIONAHA.120.15026
17. Rosendorff C, Lackland DT, Allison M, Aronow WS, Black HR, Blumenthal RS, et al. Treatment of Hypertension in Patients With Coronary Artery Disease: A Scientific Statement from the American Heart Association, American College of Cardiology, and American Society of Hypertension. J Am Coll Cardiol. 2015 May 12;65(18):1998-2038. https://doi.org/10.1016/j.jacc.2015.02.038
18. Buysschaert M, Medina JL, Buysschaert B, Bergman M. Definitions (and Current Controversies) of Diabetes and Prediabetes. Curr Diabetes Rev. 2016;12(1):8-13. https://doi.org/10.2174/1573399811666150122150233
19. MacDonald T. Prevalence of High Cholesterol Among the Adult U.S. Population: NHANES 2013–2018. Curr Dev Nutr. 2022 Jun 14;6(Suppl 1):925. https://doi.org/10.1093/cdn/nzac067.045
20. North BJ, Sinclair DA. The intersection between aging and cardiovascular disease. Circ Res. 2012 Apr 13;110(8):1097-108. https://doi.org/10.1161/CIRCRESAHA.111.246876
21. Colpani V, Baena CP, Jaspers L, van Dijk GM, Farajzadegan Z, Dhana K, et al. Lifestyle factors, cardiovascular disease and all-cause mortality in middle-aged and elderly women: a systematic review and meta-analysis. Eur J Epidemiol. 2018 Sep;33(9):831-45. https://doi.org/10.1007/s10654-018-0374-z
22. Talaei M, Sarrafzadegan N, Sadeghi M, Oveisgharan S, Marshall T, Thomas GN, et al. Incidence of cardiovascular diseases in an Iranian population: the Isfahan Cohort Study. Arch Iran Med. 2013 Mar;16(3):138-44.
23. Hartley A, Marshall DC, Salciccioli JD, Sikkel MB, Maruthappu M, Shalhoub J. Trends in Mortality From Ischemic Heart Disease and Cerebrovascular Disease in Europe: 1980 to 2009. Circulation. 2016 May 17;133(20):1916-26. https://doi.org/10.1161/CIRCULATIONAHA.115.018931
24. Wang T, Li Y, Zheng X. Association of socioeconomic status with cardiovascular disease and cardiovascular risk factors: a systematic review and meta-analysis. J Public Health (Berl.). 2024;32(3):385-99. https://doi.org/10.1007/s10389-023-01825-4
25. Lee JR, Paultre F, Mosca L. The association between educational level and risk of cardiovascular disease fatality among women with cardiovascular disease. Womens Health Issues. 2005 Mar-Apr;15(2):80-8. https://doi.org/10.1016/j.whi.2004.11.004
26. Cheng W, Zhang Z, Cheng W, Yang C, Diao L, Liu W. Associations of leisure-time physical activity with cardiovascular mortality: A systematic review and meta-analysis of 44 prospective cohort studies. Eur J Prev Cardiol. 2018 Nov;25(17):1864-72. https://doi.org/10.1177/2047487318795194
27. Taghizadeh N, Vonk JM, Boezen HM. Lifetime Smoking History and Cause-Specific Mortality in a Cohort Study with 43 Years of Follow-Up. PLoS One. 2016 Apr 7;11(4):e0153310. https://doi.org/10.1371/journal.pone.0153310
28. Chang W, Zeng Q, Zhou B. Association of education level with mortality in United States - A cross-sectional study. Acta Psychol (Amst). 2025 Mar;253:104774. https://doi.org/10.1016/j.actpsy.2025.104774
29. Lee DC, Pate RR, Lavie CJ, Sui X, Church TS, Blair SN. Leisure-time running reduces all-cause and cardiovascular mortality risk. J Am Coll Cardiol. 2014 Aug 5;64(5):472-81. https://doi.org/10.1016/j.jacc.2014.04.058
30. Hamer M, Ingle L, Carroll S, Stamatakis E. Physical activity and cardiovascular mortality risk: possible protective mechanisms? Med Sci Sports Exerc. 2012 Jan;44(1):84-8. https://doi.org/10.1249/MSS.0b013e3182251077
31. Denney JT, Rogers RG, Hummer RA, Pampel FC. Education inequality in mortality: The age and gender specific mediating effects of cigarette smoking. Soc Sci Res. 2010 Jul 1;39(4):662-73. https://doi.org/10.1016/j.ssresearch.2010.02.007