

## ORIGINAL ARTICLE

# Is there a gender gap in secondary prevention of coronary artery disease in Turkey?

## Türkiye’de koroner arter hastalığından ikincil korunmada cinsiyet etkisi var mıdır?

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### ABSTRACT

**Objective:** It has been reported that women receive fewer preventive recommendations regarding pharmacological treatment, lifestyle modifications, and cardiac rehabilitation compared with men who have a similar risk profile. This study was an investigation of the impact of gender on cardiovascular risk profile and secondary prevention measures for coronary artery disease (CAD) in the Turkish population.

**Methods:** Statistical analyses were based on the European Action on Secondary and Primary Prevention through Intervention to Reduce Events (EUROASPIRE)-IV cross-sectional survey data obtained from 17 centers in Turkey. Male and female patients, aged 18 to 80 years, who were hospitalized for a first or recurrent coronary event (coronary artery bypass graft, percutaneous coronary intervention, acute myocardial infarction, or acute myocardial ischemia) were eligible.

**Results:** A total of 88 (19.7%) females and 358 males (80.3%) were included. At the time of the index event, the females were significantly older ( $p=0.003$ ) and had received less formal education ( $p<0.001$ ). Non-smoking status ( $p<0.001$ ) and higher levels of depression and anxiety (both  $p<0.001$ ) were more common in the female patients. At the time of the interview, conducted between 6 and 36 months after the index event, central obesity ( $p<0.001$ ) and obesity ( $p=0.004$ ) were significantly more common in females. LDL-C, HDL-C or HbA1c levels did not differ significantly between genders. The fasting blood glucose level was significantly higher ( $p=0.003$ ) and hypertension was more common in females ( $p=0.001$ ). There was no significant difference in an increase in physical activity or weight loss after the index event between genders, and there was no significant difference between genders regarding continuity of antiplatelet, statin, beta blocker or ACEi/ARB II receptor blocker usage ( $p>0.05$ ).

**Conclusion:** Achievement of ideal body weight, fasting blood glucose and blood pressure targets was lower in women despite similar reported medication use. This highlights the importance of the implementation of lifestyle measures and adherence to medications in women.

### ÖZET

**Amaç:** Benzer risk profiline sahip erkekler ile kıyaslandığında, kadınlara farmakolojik tedavi, yaşam tarzı değişiklikleri ve kardiyak rehabilitasyon açısından koruyucu önerilerde daha az bulunduğu bilinmektedir. Bu çalışmada, Türk popülasyonunda kardiyovasküler risk profili ve ikincil korunma ölçütleri üzerine cinsiyetin etkisinin araştırılması hedeflenmiştir.

**Yöntemler:** İstatistiksel analiz Türkiye’de 17 merkezden elde edilen EUROASPIRE-IV (European Action on Secondary and Primary Prevention - EA-IV) kesitsel araştırma verilerine dayanarak gerçekleştirildi. İlk veya tekrarlayan koroner olay (koroner arter baypas greft, perkütan koroner girişim, akut miyokart enfarktüsü ya da akut miyokart iskemisi) nedeniyle hastaneye yatırılan 18–80 yaş aralığındaki kadın ve erkek hastalar çalışma kapsamında incelendi.

**Bulgular:** Bu çalışmaya 88 kadın (%19.7) ve 358 erkek (%80.3) dahil edildi. İlk koroner olayda, kadınların daha yaşlı ( $p=0.003$ ) ve daha az eğitilmiş ( $p<0.001$ ) oldukları saptandı. Kadınlarda sigara içiciliğinin daha az ( $p<0.001$ ), depresyon ve kaygı düzeylerinin daha yüksek (her ikisi  $p<0.001$ ) olduğu görüldü. Koroner olaydan 6–36 ay sonra yapılan görüşmede, santral obezite ( $p<0.001$ ) ve obezite ( $p=0.004$ ) kadınlarda daha sık bulundu. LDL-K, HDL-K ve HbA1c düzeyleri kadın ve erkekler arasında benzerdi. Kadınlarda kan şekeri daha yüksek ( $p=0.003$ ) ve hipertansiyon daha sık ( $p=0.001$ ) idi. Koroner olay sonrası fiziksel aktivitede artış ya da kilo kaybı cinsiyetler arasında farklı bulunmadı. Antitrombotik ilaç, statin, beta bloker ya da ACEi/ARB kullanımı bakımından da cinsiyetler arasında anlamlı farklılığa rastlanmadı ( $p>0.05$ ).

**Sonuç:** Benzer ilaç kullanım oranlarına rağmen, ideal vücut ağırlığı, açlık kan şekeri ve kan basıncı değerlerine ulaşma oranı kadınlarda daha düşük saptanmıştır. Bu bulgu, kadınlarda yaşam tarzı değişiklikleri ve ilaç tedavisine uyumun önemine vurgu yapmaktadır.

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Awareness of the importance of coronary artery disease (CAD) as a cause of mortality in women has increased in the last decade.<sup>[1]</sup> Its impact on women's health had previously been underappreciated due to the higher incidence of CAD at younger ages in men. However, it is now known that CAD mortality is higher in women than in men.<sup>[2]</sup> Several papers have suggested that gender-based differences exist regarding secondary prevention of CAD. Unfortunately, women are known to receive fewer preventive recommendations regarding both lifestyle modifications and pharmacological treatment compared with men who have a similar risk profile.<sup>[3-7]</sup> Furthermore, cardiac rehabilitation after myocardial infarction (MI) has been reported to be underused in women.<sup>[8-11]</sup>

The recently published Türk Erişkinlerinde Kalp Hastalığı ve Risk Faktörleri (TEKHARF) survey revealed a higher CAD mortality in men (5.7/1000 vs. 3.6/1000 individuals per year), but a higher incidence of CAD in women between 1998 and 2014 (16.2/1000 vs. 15.2/1000 individuals per year).<sup>[12]</sup> Despite a lower CAD mortality compared with Turkish men, CAD mortality in Turkish women is known to be the highest among European countries.<sup>[13,14]</sup> These data suggest the emergent need for the implementation of prevention measures for CAD in women.

The aim of this study was to investigate the impact of gender on determinants of secondary prevention measures in the Turkish population.

## METHODS

Analyses were based on the European Action on Secondary and Primary Prevention through Intervention to Reduce Events (EUROASPIRE, EA)-IV cross-sectional survey (2012–2013) data obtained from 17 centers in Turkey.<sup>[15]</sup> Males and females aged 18 to 80 years who were hospitalized for a first or recurrent coronary event (coronary artery bypass grafting [CABG], percutaneous coronary intervention [PCI], acute MI [AMI], or acute myocardial ischemia) were eligible for inclusion in the survey. Data collection was performed by trained research staff. Written informed consent was obtained from each participant.

Information on personal and demographic details, co-morbidities, medications, smoking status, and anthropometric measurements were obtained from med-

ical records. The patients were examined and interviewed (self-reported information on lifestyle, other risk factor management, and medication) between 6 months and 3 years after the recruiting diagnosis.

### Abbreviations:

ACE	Angiotensin converting-enzyme
AMI	Acute myocardial infarction
BMI	Body mass index
CABG	Coronary artery bypass grafting
CAD	Coronary artery disease
EA	EUROASPIRE (European Action on Secondary and Primary Prevention through Intervention to Reduce Events)
HbA1c	Glycated hemoglobin
HDL-C	High-density lipoprotein-cholesterol
LDL-C	Low-density lipoprotein-cholesterol
MI	Myocardial infarction
PCI	Percutaneous coronary intervention

Being overweight or obese was defined as having a body mass index (BMI)  $\geq 25$  kg/m<sup>2</sup> or  $\geq 30$  kg/m<sup>2</sup>, respectively. Central obesity was defined as a waist circumference  $\geq 102$  cm in males and  $\geq 88$  cm in females. A high-density lipoprotein-cholesterol (HDL-C) level not on target was defined as  $< 40$  mg/dL in male and  $< 45$  mg/dL in females. Low-density lipoprotein-cholesterol (LDL-C) that was not on target was defined as a level of  $\geq 70$  mg/dL. Diabetes was defined as a fasting blood glucose value of  $\geq 126$  mg/dL. Hypertension was defined as a systolic blood pressure measurement of  $\geq 140$  ( $\geq 130$  in diabetic patients) and/or diastolic blood pressure  $\geq 90$  ( $\geq 80$  in diabetic patients) mm Hg. In addition, the EUROASPIRE-III (EA-III) data were used to compare the prevalence of cardiovascular risk factors in the Turkish population with that identified in the EA-IV. The EA-III survey was carried out between 2006 and 2007, and the data were obtained from the same 17 centers in Turkey. The diagnostic criteria for inclusion were similar to those of the EA-IV.

### Statistical analysis

The data were analyzed using PASW Statistics for Windows, Version 18.0 (SPSS Inc., Chicago, IL, USA). Descriptive statistics were expressed as numbers and percentages for categorical variables and as mean  $\pm$  standard deviation or median (percentile 25 [Q1]- percentile 75 [Q3]) for numerical variables. The numerical variables were investigated using the Kolmogorov-Smirnov test to determine if there was normal distribution. For categorical variables, a chi-square test was used in 2 groups and multiple comparisons when the chi-square condition was met. Continuity correction and Fisher's exact tests were used for multiple comparisons when the chi-square

condition was not met. For the comparison of 2 independent groups, the Mann-Whitney U test was used for non-normally distributed numerical variables. To test the significance of pairwise differences, a chi-square test or continuity correction and Fisher's exact tests followed with the Bonferroni correction to adjust for multiple comparisons were performed. A type-I error level of less than 5% was used to infer statistical significance.

## RESULTS

In the Turkey arm of the EA-IV, 446 consecutive male or female patients aged 18 to 80 years were identified following the diagnosis of first or recurrent CAD occurring 6 to 36 months preceding the interview: (i) CABG, (ii) PCI, (iii) AMI, or (iv) acute myocardial ischemia. There was a total of 88 (19.7%) female patients. There was no statistically significant differ-

**Table 1. Comparison of cardiovascular risk profile in males and females at the time of the index event (n=446)**

	Total (n=446)		Female (n=88) (19.7%)		Male (n=358) (80.3%)		p
	N	n (%)	N	n (%)	N	n (%)	
Age, years							
Median (Q1-Q3)	446	58.8 (52.3–66.3)	88	62.4 (53.6–69.6)	358	58.2 (51.5–65.1)	0.003*
Age groups, n (%)	446		88		358		
<50 years <sup>d</sup>		86 (19.3)		10 (11.4)		76 (21.2)	
50–59 years		155 (34.8)		27 (30.7)		128 (35.8)	0.012*
60–69 years		133 (29.8)		28 (31.8)		105 (29.3)	
≥70 years <sup>a</sup>		72 (16.1)		23 (26.1)		49 (13.7)	
Education status, n (%)							
More than primary school completed	229	128 (55.9)	37	6 (16.2)	192	122 (63.5)	<0.001*
BMI ≥25 kg/m <sup>2</sup>	230	186 (80.9)	46	38 (82.6)	184	148 (80.4)	0.737
BMI ≥30 kg/m <sup>2</sup>	230	73 (31.7)	46	20 (43.5)	184	53 (28.8)	0.056
LDL-C level not on target, n (%)	391	349 (89.3)	75	67 (89.3)	316	282 (89.2)	1.000
HDL-C level not on target, n (%)	386	219 (56.7)	75	48 (64.0)	311	171 (55.0)	0.157
Diabetes mellitus, n (%)	356	125 (35.1)	74	29 (39.2)	282	96 (34)	0.409
Hypertension, n (%)	372	169 (45.4)	73	34 (46.6)	299	135 (45.2)	0.826
Smoking status, n (%)	326		66		260		
Current smoker <sup>4</sup>		104 (31.9)		11 (16.7)		93 (35.8)	
Has stopped smoking <sup>4</sup>		73 (22.4)		6 (9.1)		67 (25.8)	<0.001*
Is a current non-smoker <sup>4</sup>		53 (16.3)		4 (6.1)		49 (18.8)	
Non-smoker <sup>1,2,3</sup>		96 (29.4)		45 (68.2)		51 (19.6)	
HADS subscales	187		28		159		
HADS-Anxiety, Median (Q1-Q3)		6 (4–9)		9 (6–12.5)		6 (4–8)	<0.001*
HADS-Depression, Median (Q1-Q3)		6 (4–9)		10 (6.5–12.5)		6 (3–9)	<0.001*

BMI: Body mass index; HADS: Hospital Anxiety and Depression Scale; HDL-C: High-density lipoprotein-cholesterol; LDL-C: Low-density lipoprotein-cholesterol; Q: Quartile.

\*a p value <0.05 denotes statistical significance.

<sup>a</sup><50 years; <sup>b</sup>50–59 years; <sup>c</sup>60–69 years; <sup>d</sup>≥70 years.

<sup>1</sup>Current smoker; <sup>2</sup>Has stopped smoking; <sup>3</sup>Is a current non-smoker; <sup>4</sup>Non-smoker.

ence concerning the type of index event (CABG, PCI, AMI, ischemia) between male and female patients ( $p=0.681$ ).

Table 1 illustrates the comparison of males and females in terms of their cardiovascular risk profile at the time of the index event. At the time of index event, females were significantly older than males ( $p=0.003$ ). When age groups (<50, 50–59, 60–69,  $\geq 70$  years) were compared, the ratio of males who experienced the index event at an age younger than 50 was significantly higher than that of females (21.2 vs. 11.4%;  $p=0.012$ ). Only 1 female (2.7%) had completed university, whereas 35 males (18.2%) had completed university. Most of the females (37.8%) had not had formal education. When compared with that of males, the ratio of females who completed education beyond primary school was significantly lower (6 [16.2%] vs. 122 [63.5%];  $p<0.001$ ). Concerning other cardiovascular risk factors at the time of the index event, BMI, LDL-C or HDL-C levels did not differ significantly between genders (all  $p>0.05$ ). The prevalence of patients diagnosed with diabetes mellitus and hypertension was also similar (all  $p>0.05$ ). Non-smoking status was significantly more common in females compared with males (68.2 vs. 19.6%;

$p<0.001$ ). Females had significantly higher levels of depression (10 [6.5–12.5] vs. 6 [3–9];  $p<0.001$ ) and anxiety (9 [6–12.5] vs. 6 [4–8];  $p<0.001$ ) compared with males.

Comparison of males and females regarding their cardiovascular risk profile at the time of the interview undertaken 6 to 36 months following the index event is shown in Table 2. Central obesity (85.3 vs. 41.8%;  $p<0.001$ ) and obesity (62.9 vs. 36.8%;  $p=0.007$ ) were significantly more common in females compared with males. LDL-C, HDL-C or HbA1c levels did not differ between males and females (all  $p>0.05$ ). However, more females were found to have a higher fasting blood glucose level (51.6 vs. 25.5%,  $p=0.006$ ). Hypertension was also more common in females (69.4 vs. 40.6%;  $p=0.002$ ), whereas smoking, defined as self-reported smoking at the time of interview or carbon monoxide in the breath  $>10$  ppm, was more common in males (28.7 vs. 8.1%;  $p=0.015$ ). An increase in physical activity or weight loss after the index event did not differ between genders (all  $p>0.05$ ). In addition, continuation of medical treatment with antiplatelets, statins, beta blockers or angiotensin-converting enzyme (ACE) inhibitors/angiotensin II receptor blockers was similar ( $p>0.05$ ).

**Table 2.** Comparison of cardiovascular risk profile in males and females at the time of the interview undertaken 6–36 months following the index event (n=239)

	Total (n=239)		Female (n=37)		Male (n=202)		p
	N	n (%)	N	n (%)	N	n (%)	
Central obesity	230	111 (48.3)	34	29 (85.3)	196	82 (41.8)	<0.001*
BMI $\geq 25$ kg/m <sup>2</sup>	236	191 (80.9)	35	31 (88.6)	201	160 (79.6)	0.311
BMI $\geq 30$ kg/m <sup>2</sup>	236	96 (40.7)	35	22 (62.9)	201	74 (36.8)	0.007*
LDL-C level not on target	217	199 (91.7)	35	35 (100)	182	164 (90.1)	0.108
HDL-C level not on target	228	131 (57.5)	35	21 (60)	193	110 (57)	0.885
Fasting blood glucose $\geq 126$ mg/dL	219	64 (29.2)	31	16 (51.6)	188	48 (25.5)	0.006*
HbA1c $\geq 7\%$	223	67 (30.0)	34	14 (41.2)	189	53 (28)	0.182
Hypertension	238	107 (45)	36	25 (69.4)	202	82 (40.6)	0.002*
Smoking status <sup>a</sup>	239	61 (25.5)	37	3 (8.1)	202	58 (28.7)	0.015*
Trying to do more physical activities	236	92 (39)	36	15 (41.7)	200	77 (38.5)	0.863
More every day physical activities	239	105 (43.9)	36	16 (44.4)	196	89 (45.4)	1.000
Weight loss <sup>b</sup>	139	60 (43.2)	21	11 (52.4)	118	49 (41.5)	0.493

BMI: Body mass index; HbA1c: Glycated hemoglobin; HDL-C: High-density lipoprotein-cholesterol; LDL-C: Low-density lipoprotein-cholesterol.

\*a p value <0.05 denotes statistical significance. <sup>a</sup>Smoking status was determined as self-reported smoking at the time of the interview or carbon monoxide in the breath  $>10$  ppm. <sup>b</sup>Weight loss since the index event and before the interview.

**Table 3.** Comparison of the cardiovascular risk profile at the time of the index event between females participating in the EUROASPIRE-III and IV

	EA-IV females (n=88) (35.6%)		EA-III females (n=159) (64.4%)		p
	N	n (%)	N	n (%)	
Education					
More than primary school completed	37	6 (16.2)	65	7 (10.8)	0.539
Primary school or less completed		31 (83.8)		58 (89.2)	
Age (years) Median (Q1-Q3)	88	62.4 (53.6–69.6)	159	66.0 (58.7–71.4)	0.024*
Age groups					
<50 years	88	10 (11.4)	159	12 (7.5)	0.309
50–59 years		27 (30.7)		36 (22.6)	
60–69 years		28 (31.8)		62 (39.0)	
≥70 years		23 (26.1)		49 (30.8)	
BMI ≥25 kg/m <sup>2</sup>	46	38 (82.6)	28	25 (89.3)	0.655
BMI ≥30 kg/m <sup>2</sup>	46	20 (43.5)	28	16 (57.1)	0.368
LDL-C level not on target	75	67 (89.3)	87	76 (87.4)	0.885
HDL-C level not on target	75	48 (64.0)	87	44 (50.6)	0.085
Diabetes mellitus	74	29 (39.2)	91	45 (49.5)	0.187
Hypertension	73	34 (46.6)	121	72 (59.5)	0.080
Smoking status					
Current smoker	66	11 (16.7)	133	25 (18.8)	0.637
Has stopped smoking		6 (9.1)		11 (8.3)	
Is a current non-smoker		4 (6.1)		15 (11.3)	
Non-smoker		45 (68.2)		82 (61.7)	

BMI: Body mass index; EUROASPIRE: European Action on Secondary and Primary Prevention through Intervention to Reduce Events; HDL-C: High-density lipoprotein-cholesterol; LDL-C: Low-density lipoprotein-cholesterol; Q: Quartile.

\*a p value <0.05 denotes statistical significance.

A total of 669 patients (510 men and 159 women) were included in the EA-III and 338 patients (50.5%) were interviewed at least 6 months after the index event. A comparison of EA-IV and EA-III data regarding the cardiovascular risk profile in females at the time of index event is shown in Table 3. At the time of the index event, LDL-C, HDL-C, BMI, fasting blood glucose, smoking status and blood pressure values were similar in females participating in the EA-III and EA-IV (all  $p>0.05$ ). Females in the EA-III were older than those included in the EA-IV ( $p=0.024$ ) (Table 3). The presence of 3 or more cardiovascular risk factors was not found to be significantly associated with gender neither at the time of the index event (47.1 vs. 43.8;  $p=0.574$ ) or interview (78.4 vs. 62.9%;  $p=0.069$ ) among EA-IV participants, although it was numerically greater in females. However, among the

EA-III participants, more females were found to have 3 or more cardiovascular risk factors at the time of the interview (81.5 vs. 56%;  $p<0.001$ ), but not at that of the index event (26.7 vs. 27.2%;  $p=0.894$ ).

Comparison of target achievement in males and females among participants of the EA-IV is shown in Table 4. The percentage of females who reached their blood pressure target was significantly lower than that of males (22.2 vs. 53.4%;  $p=0.031$ ). Target achievement for other cardiovascular risk factors did not differ between genders (all  $p>0.05$ ). Changes in LDL-C, HDL-C, HbA1c or fasting blood glucose levels did not differ with respect to education level (having completed more than primary school vs. primary school or less) or age at the index event (<65 vs. ≥65 years) in females (all  $p>0.05$ ). Target achievement concerning

**Table 4. Comparison of target achievement in males and females among participants of EUROASPIRE-IV**

	Total		Female		Male		p
	N	n (%)	N	n (%)	N	n (%)	
Body mass index: Overweight	105		16		89		
<25 kg/m <sup>2</sup>		13 (12.4)		1 (6.3)		12 (13.5)	0.686
≥25 kg/m <sup>2</sup>		92 (87.6)		15 (93.8)		77 (86.5)	
Body mass index: Obese	37		6		31		
<30 kg/m <sup>2</sup>		10 (27)		0 (0)		10 (32.3)	0.162
≥30 kg/m <sup>2</sup>		27 (73)		6 (100)		21 (67.7)	
Low-density lipoprotein-cholesterol	171		28		143		
<70 mg/dL		10 (5.8)		0 (0)		10 (7)	0.371
≥70 mg/dL		161 (94.2)		28 (100)		133 (93)	
High-density lipoprotein-cholesterol	105		19		86		
≥40 mg/dL (M)/45 mg/dL (F)		14 (13.3)		3 (15.8)		11 (12.8)	0.715
<40 mg/dL (M)/45 mg/dL (F)		91 (86.7)		16 (84.2)		75 (87.2)	
Fasting blood glucose	62		13		49		
<126 mg/dL		22 (35.5)		2 (15.4)		20 (40.8)	0.112
≥126 mg/dL		40 (64.5)		11 (84.6)		29 (59.2)	
Hypertension	106		18		88		
<140/90							
<130/80 (diabetics)		51 (48.1)		4 (22.2)		47 (53.4)	0.031*
≥140/90							
≥130–80 (diabetics)		55 (51.9)		14 (77.8)		41 (46.6)	

EUROASPIRE: European Action on Secondary and Primary Prevention through Intervention to Reduce Events; F: Female; M: Male.

\*a p value <0.05 denotes statistical significance.

BMI, LDL-C, HDL-C, HbA1c, fasting blood glucose or blood pressure in females also did not significantly differ according to education level (having completed more than primary school vs. primary school or less) or age at the index event (<65 vs. ≥65 years) in females (all p>0.05). In addition, target achievement in cardiovascular risk factors among females was not influenced by neither age or educational status at the time of the index event (all p>0.05). Changes in LDL-C, HDL-C, HbA1c, or fasting blood glucose levels that were observed at follow-up in females were also not associated with age or educational status at the time of the index event (all p>0.05).

## DISCUSSION

The EUROASPIRE-IV Turkish arm data revealed a large gap between males and females regarding secondary prevention measures. Our findings indicate that except for smoking less and being older, and

unfortunately being undereducated at the time of the index event, the clinical cardiovascular risk profile in females was similar to that of males at the time of the index event. However, despite the similarity at the time of the index event, a difference in the prevalence of central obesity, obesity, higher fasting blood glucose levels and hypertension that favored males was observed at follow-up. Target achievement in females regarding obesity, fasting blood glucose levels, and blood pressure was significantly insufficient at the time of the follow-up interview. Regrettably, despite the 6-year interval between the EA-III and EA-IV surveys, neither the education status, nor the clinical cardiovascular risk profile seemed to improve in females.

Coronary artery disease results in more adverse events in women than in men. Among individuals 45 to 64 years of age, women have been found to be more likely to suffer from heart failure following MI<sup>[2]</sup> and anginal episodes.<sup>[2,16]</sup> Cardiovascular risk factor mod-

ification after the index event is essential to reduce the associated morbidity and mortality. The EA-IV cross-sectional survey data obtained from 24 European countries has demonstrated a significantly worse risk factor profile in females compared with males, reflected in a higher prevalence of having 3 or more cardiovascular risk factors across all age groups at the time of the index event.<sup>[17]</sup> At the time of the interview, the prevalence of 3 or more cardiovascular risk factors was numerically greater in the Turkish women included in the EA-IV compared with the men. This finding had reached statistical significance in the EA-III. The failure to reach statistical significance in the current EA-IV survey may be explained by the fact that the number of female participants was relatively smaller in the EA-IV compared with the EA-III.

The findings of the EA-IV Turkish survey indicate that although similar at the time of the index event in terms of having 3 or more cardiovascular risk factors, a difference in the prevalence of central obesity and obesity, higher fasting blood glucose levels and hypertension between genders that favored males was apparent at the follow-up. This may be due to several factors, including older age at diagnosis, lower education status and psychosocial factors (reflected in higher anxiety and depression scores). Along with the global problems in women's health, such as low compliance with lifestyle advice, failure to maintain lifestyle modifications and underutilization of evidence-based medical and interventional therapies, these factors may lead to the gender gap in secondary prevention.

Turkish women were more likely to be non-smokers, both at the time of the index event and the interview, as in other European countries. Obesity and LDL-C, fasting blood glucose and HbA1c values that were not on target were more common in women in Turkey, similar to the findings in other European countries.<sup>[17]</sup> Although no significant difference in terms of reaching the target blood pressure was observed in other European countries,<sup>[17]</sup> Turkish women were more likely to have higher blood pressure values compared with males at the time of the interview.

The EUROASPIRE-IV cross-sectional survey data obtained from 24 European countries revealed that females had a significantly lower education level and were older at the time of the index event compared with males, which is consistent with our findings.

<sup>[17]</sup> Older age at the time of the index event may be a limiting factor in target achievement in secondary prevention. Less education in women may also lead to lower awareness.<sup>[18]</sup> Although age and education status were significantly associated with having 3 or more cardiovascular risk factors in the European survey,<sup>[17]</sup> our results did not demonstrate such a relationship. This may be due to the relatively small number of women included in the survey in the Turkish arm of the EA-IV.

Compliance with lifestyle advice and adherence to physical activity advice or weight change recommendations did not differ significantly between genders in the Turkish population, which was similar to what was observed in other European countries.<sup>[17]</sup> However, females were still found to be more obese at the time of the interview, despite the lack of a significant difference regarding weight loss or attempt for physical activity between genders. Social barriers existing in many countries may restrict women from the adoption of healthy lifestyle habits. In addition, women are known to be less likely to maintain a healthy lifestyle status due to household and caretaking responsibilities or comorbidities (such as osteoarthritis, osteoporosis), particularly in the postmenopausal period. Lack of access to healthy food and fitness facilities and living in a dangerous neighborhood that restricts outdoor physical activity are among the factors that may limit the improvement of cardiovascular risk factors, particularly in low-income women. Furthermore, women are known to be less successful in coping with depression, anger, stress or boredom compared with males. The higher anxiety and depression levels that we detected in Turkish females may have contributed to the failure in target achievement and cardiovascular risk factor reduction.

Previous studies have suggested that women are prescribed fewer medications for secondary prevention than men. African American or Hispanic women, especially if older, are less likely than white men to receive aspirin, beta blocker, ACE inhibitor or lipid-lowering drugs after MI, despite evidence of benefit.<sup>[19,20]</sup> These patients are also less likely to be referred for revascularization procedures<sup>[21,22]</sup> and cardiac rehabilitation.<sup>[8-11]</sup> The Canadian Acute Coronary Syndrome Registry, which assessed factors influencing the underutilization of evidence-based therapies in women,<sup>[23]</sup> has shown lower rates of ACE inhibitor, beta blocker,

and lipid-lowering drug use among women, which correlated with older age. Despite adjustment for biasing confounders, female gender remained associated with underutilization of guideline-based therapy with lipid-lowering drugs and ACE inhibitors. In our study, the reported medication use did not significantly differ between genders in the Turkish population, which was consistent with other European countries.<sup>[17]</sup> Previous studies have shown that women are less likely to adhere to medications.<sup>[24]</sup> Our findings do not necessarily reflect compliance with medications.

### Limitations

The limited number of women in the study population resulted in failure to reach statistical significance in several statistical analyses. Second, the survey was undertaken in patients from only 3 metropolitan cities. Finally, although a standardized and detailed survey was conducted, data related to physical activity and dietary habits of the patients were based only on patients' own statements.

### Conclusion

Our findings demonstrated that secondary prevention measure implementation is insufficient in females compared with males in Turkey, particularly when achievement of ideal body weight and fasting blood glucose and blood pressure targets are concerned. The lack of a significant difference regarding the use of prescribed drugs between genders draws attention to the importance of adherence to healthy lifestyle habits and the efficient use of cardiac rehabilitation to improve outcomes in females. Older age at the time of the index event and psychosocial stress may pose a problem in the adoption of healthy lifestyle habits in females. Therefore, promotion of healthy life habits should be initiated early in childhood.

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## REFERENCES

1. Mosca L, Mochari-Greenberger H, Dolor RJ, Newby LK, Robb KJ. Twelve-year follow-up of American women's awareness of cardiovascular disease risk and barriers to heart health. *Circ Cardiovasc Qual Outcomes* 2010;3:120-7. [\[CrossRef\]](#)
2. Roger VL, Go AS, Lloyd-Jones DM, Benjamin EJ, Berry JD, Borden WB, et al. Heart disease and stroke statistics--2012 update: a report from the American Heart Association. *Circulation* 2012;125:e2-220.
3. Mosca L, Linfante AH, Benjamin EJ, Berra K, Hayes SN, Walsh BW, et al. National study of physician awareness and adherence to cardiovascular disease prevention guidelines.



- Circulation 2005;111:499–510. [\[CrossRef\]](#)
4. Abuful A, Gidron Y, Henkin Y. Physicians' attitudes toward preventive therapy for coronary artery disease: is there a gender bias? *Clin Cardiol* 2005;28:389–93. [\[CrossRef\]](#)
  5. Chou AF, Scholle SH, Weisman CS, Bierman AS, Correa-de-Araujo R, Mosca L. Gender disparities in the quality of cardiovascular disease care in private managed care plans. *Womens Health Issues* 2007;17:120–30. [\[CrossRef\]](#)
  6. Gu Q, Burt VL, Paulose-Ram R, Dillon CF. Gender differences in hypertension treatment, drug utilization patterns, and blood pressure control among US adults with hypertension: data from the National Health and Nutrition Examination Survey 1999–2004. *Am J Hypertens* 2008;21:789–98. [\[CrossRef\]](#)
  7. Bird CE, Fremont AM, Bierman AS, Wickstrom S, Shah M, Rector T, et al. Does quality of care for cardiovascular disease and diabetes differ by gender for enrollees in managed care plans? *Womens Health Issues* 2007;17:131–8. [\[CrossRef\]](#)
  8. Witt BJ, Jacobsen SJ, Weston SA, Killian JM, Meverden RA, Allison TG, et al. Cardiac rehabilitation after myocardial infarction in the community. *J Am Coll Cardiol* 2004;44:988–96. [\[CrossRef\]](#)
  9. Suaya JA, Shepard DS, Normand SL, Ades PA, Prottas J, Stason WB. Use of cardiac rehabilitation by Medicare beneficiaries after myocardial infarction or coronary bypass surgery. *Circulation* 2007;116(1):1653–62.
  10. Evenson KR, Rosamond WD, Luepker RV. Predictors of outpatient cardiac rehabilitation utilization: the Minnesota Heart Surgery Registry. *J Cardiopulm Rehabil* 1998;18:192–8. [\[CrossRef\]](#)
  11. Thomas RJ, Miller NH, Lamendola C, Berra K, Hedbäck B, Durstine JL, et al. National Survey on Gender Differences in Cardiac Rehabilitation Programs. Patient characteristics and enrollment patterns. *J Cardiopulm Rehabil* 1996;16:402–12.
  12. Onat A, Karakoyun S, Akbaş T, Karadeniz FÖ, Karadeniz Y, Çakır H, et al. Turkish Adult Risk Factor survey 2014: Overall mortality and coronary disease incidence in Turkey's geographic regions. *Turk Kardiyol Dern Ars* 2015;43:326–32.
  13. Müller-Nordhorn J, Binting S, Roll S, Willich SN. An update on regional variation in cardiovascular mortality within Europe. *Eur Heart J* 2008;29:1316–26. [\[CrossRef\]](#)
  14. Sans S, Kesteloot H, Kromhout D. The burden of cardiovascular diseases mortality in Europe. Task Force of the European Society of Cardiology on Cardiovascular Mortality and Morbidity Statistics in Europe. *Eur Heart J* 1997;18:1231–48.
  15. Tokgözoğlu L, Kayıkçıoğlu M, Altay S, Aydoğdu S, Barçın C, Bostan C, et al. EUROASPIRE-IV: European Society of Cardiology study of lifestyle, risk factors, and treatment approaches in patients with coronary artery disease: Data from Turkey. *Turk Kardiyol Dern Ars* 2017;45:134–44.
  16. Hemingway H, Langenberg C, Damant J, Frost C, Pyörälä K, Barrett-Connor E. Prevalence of angina in women versus men: a systematic review and meta-analysis of international variations across 31 countries. *Circulation* 2008;117:1526–36. [\[CrossRef\]](#)
  17. De Smedt D, De Bacquer D, De Sutter J, Dallongeville J, Gevaert S, De Backer G, et al. The gender gap in risk factor control: Effects of age and education on the control of cardiovascular risk factors in male and female coronary patients. The EUROASPIRE IV study by the European Society of Cardiology. *Int J Cardiol* 2016;209:284–90. [\[CrossRef\]](#)
  18. Stringhini S, Spencer B, Marques-Vidal P, Waeber G, Vollenweider P, Paccaud F, et al. Age and gender differences in the social patterning of cardiovascular risk factors in Switzerland: the CoLaus study. *PLoS One* 2012;7:e49443. [\[CrossRef\]](#)
  19. Herholz H, Goff DC, Ramsey DJ, Chan FA, Ortiz C, Labarthe DR, et al. Women and Mexican Americans receive fewer cardiovascular drugs following myocardial infarction than men and non-Hispanic whites: the Corpus Christi Heart Project, 1988–1990. *J Clin Epidemiol* 1996;49:279–87. [\[CrossRef\]](#)
  20. Krumholz HM, Radford MJ, Ellerbeck EF, Hennen J, Meehan TP, Petrillo M, et al. Aspirin for secondary prevention after acute myocardial infarction in the elderly: prescribed use and outcomes. *Ann Intern Med* 1996;124:292–8. [\[CrossRef\]](#)
  21. Bearden D, Allman R, McDonald R, Miller S, Pressel S, Petrovitch H. Age, race, and gender variation in the utilization of coronary artery bypass surgery and angioplasty in SHEP. SHEP Cooperative Research Group. Systolic Hypertension in the Elderly Program. *J Am Geriatr Soc* 1994;42:1143–9. [\[CrossRef\]](#)
  22. Gan SC, Beaver SK, Houck PM, MacLehose RF, Lawson HW, Chan L. Treatment of acute myocardial infarction and 30-day mortality among women and men. *N Engl J Med* 2000;343:8–15. [\[CrossRef\]](#)
  23. Bugiardini R, Yan AT, Yan RT, Fitchett D, Langer A, Manfrini O, et al. Factors influencing underutilization of evidence-based therapies in women. *Eur Heart J* 2011;32:1337–44. [\[CrossRef\]](#)
  24. Mann DM, Woodward M, Muntner P, Falzon L, Kronish I. Predictors of nonadherence to statins: a systematic review and meta-analysis. *Ann Pharmacother* 2010;44:1410–21. [\[CrossRef\]](#)
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