



Original Article

Associated Factors of Ischemic Heart Disease Identified Among Post-Menopausal Women



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ABSTRACT

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Objectives: This study identifies associated factors of ischemic heart disease (IHD) among post-menopausal Korean women at the biomedical (age, family history of hypertension, dyslipidemia, type 2 diabetes mellitus, or cerebro-cardiovascular disease, body mass index, and metabolic syndrome), biosocial (socioeconomic status and educational level), and psychosocial levels (stress, depression, smoking, binge alcohol consumption, and physical activity).

Methods: This study used a cross-sectional design with secondary data analysis of the 2013–2016 Korean National Health and Nutrition Examination Survey. Data from 3,636 women were analyzed by logistic regression analysis using a complex sample procedure.

Results: Of the biomedical factors, older age [odds ratio (OR): 2.99, 95% confidence interval (CI): 1.87–4.80, $p < 0.001$], family history (OR: 2.29, 95% CI: 1.44–3.65, $p = 0.001$), and metabolic syndrome (OR: 1.93, 95% CI: 1.27–2.95, $p = 0.002$) were associated with IHD in post-menopausal women. Of the psychosocial factors, depression (OR: 2.56, 95% CI: 1.66–3.96, $p < 0.001$) and smoking (OR: 1.92, CI: 1.04–3.55, $p = 0.038$) were associated with IHD in post-menopausal women.

Conclusion: These findings suggest that healthcare providers need to consider the contributing adverse effects of older age, family history, metabolic syndrome, depression and smoking when evaluating risk factors for IHD in post-menopausal women.

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Introduction

Ischemic heart disease (IHD) is a cardiovascular disease characterized by a narrowed or clogged coronary artery, including angina pectoralis and myocardial infarction [1]. Globally, the prevalence of IHD increases with age and poor lifestyle, such as high-fat and high-calorie diets, insufficient physical activity, smoking, and heavy alcohol consumption. It has been the primary cause of death worldwide for the past 15 years [2]. As IHD is a major cause of increasing mortality among Korean adults over 40 years old, mortality due to IHD increased from 41.1 per 100,000 people in 2006, to 58.2 per

100,000 people in 2016, and it was the second leading cause of death among Korean adults in 2016 [3]. Thus, middle-aged individuals (over 40 years) should be concerned about the associated factors of IHD.

In particular, middle-aged women over 40 years are the group at greatest risk of IHD with complications due to an alteration in hormone levels associated with menopause, and the accumulation of body fat, such as abdominal obesity due to aging [1]. Post-menopausal women also showed a greater increase in systolic blood pressure, and total cholesterol and triglyceride levels, as well as low density lipoprotein associated with development of cardiovascular disease, including

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coronary artery disease [4]. In a previous study, mortality and morbidity associated with IHD among post-menopausal women was higher than that of men in the same age group [5]. This was due to weakened protective effects against cardiovascular disease associated with estrogen deficiency. However, pre-menopausal women showed a lower prevalence of mortality and morbidity associated with IHD than men in the same age group [5]. Thus, early intervention, including detection of risk factors for IHD, would be required to decrease mortality and morbidity associated with IHD among post-menopausal women as this group may be considered as an at-risk population. In particular, risk factors of IHD are different according to gender due to differences in microvascular function [6]. In addition, components of metabolic syndrome among women were more significantly associated with the development of IHD than those of men [7]. Thus, the specific factors associated with IHD among women need to be identified.

In previous studies, the factors identified as being associated with IHD were mainly biological factors, such as age [8] and the components of metabolic syndrome [9]. However, the development of IHD has also been associated with various psychosocial factors, including emotional distress and socioeconomic status [10]. Thus, the identification of the associated factors of IHD in post-menopausal women is multidimensional, including both biological and psychological characteristics.

The biopsychosocial model developed by Hoffman and Driscoll [11] has been considered a framework for the holistic approach to health status, and was appropriate for identification of potential biomedical (e.g., genetics, biological processes, disease symptoms), biosocial (e.g., race/ethnicity, gender, socioeconomic status, and environment), and psychosocial factors (e.g., mood, behaviors, social support) associated with IHD. A literature review revealed that biomedical factors associated with an increased risk of IHD were increasing age [8], family history of hypertension, dyslipidemia, Type 2 diabetes mellitus (T2DM) or cerebrocardiovascular disease [8], being overweight or obese [1], and metabolic syndrome [4]. In addition, biosocial factors such as, low educational level and socioeconomic status, were associated with an increased risk of IHD [12]. Finally, psychosocial factors such as, depression [13], high level of emotional stress [14], having previously smoked [8,15], binged on alcohol [15], and had a low level of physical activity [14] were associated factors for IHD.

Thus, associated factors of IHD among post-menopausal Korean women at the biomedical, biosocial, and psychosocial levels were identified.

Materials and Methods

1. Study design and samples

This study used a cross-sectional design with secondary data analysis of the 2013-2016 Korean National Health and Nutrition Examination Survey (KNHANES). The KNHANES is a nationwide survey that evaluates the health and nutritional status of the Korean population. In this survey 41,102 people were selected by stratified sampling method. Samples for data analysis included post-menopausal women older than 40 years of age who had completed a questionnaire that assessed health and nutritional status and had undergone a physical examination. Ultimately, data from 3,636 women were analyzed.

2. Ethics statement

The KNHANES was approved by the Korea Centers for Disease Control and Prevention's Institutional Review Board (IRB No. 2013-12EXP-03-5C), and all participants provided written informed consent. This study adhered to the tenets of the Declaration of Helsinki.

3. Measurements

3.1. Outcome variable

3.1.1. IHD

The presence of IHD was assessed by asking participants the following question, "Do you have angina pectoralis or myocardial infarction diagnosed by a cardiologist?" The available responses were "yes" or "no."

3.2. Independent variables

3.2.1. Biomedical factors

In terms of biomedical factors, age was categorized into more than 40 years - less than 65 years, and more than 65 years. Family history of hypertension, dyslipidemia, T2DM or cerebrocardiovascular disease were assessed by asking the following question, "Have any of your direct family members been diagnosed with hypertension, dyslipidemia, T2DM, or cerebrocardiovascular disease by a cardiologist?" Available responses were "yes" or "no." Body mass index was calculated with height and weight by measured standardized instruments in kilograms, divided by the height in meters squared (m^2). Body mass index was classified into underweight ($< 18.5 \text{ kg}/m^2$), normal weight ($\geq 18.5 \text{ kg}/m^2$ and $< 23 \text{ kg}/m^2$), overweight ($\geq 23 \text{ kg}/m^2$ and $< 25 \text{ kg}/m^2$), or obese ($\geq 25 \text{ kg}/m^2$) using the criteria recommended by the Korean Society for the Study of Obesity [16]. Metabolic syndrome was defined in accordance with the clinical diagnostic criteria established by the American Heart Association and the National Heart, Lung, and Blood Institute [17]. For evaluation of waist circumference, the study used criteria from the Korean Society for the Study of Obesity

[18]. Metabolic syndrome was diagnosed when more than 3 out of the following 5 components were present; 1) waist circumference ≥ 85 cm in women, 2) blood pressure $\geq 130/85$ mmHg, or taking medication for treatment of hypertension, 3) high-density lipoprotein cholesterol levels < 50 mg/dL in women, or use of medications to decrease levels of high-density lipoprotein cholesterol, 4) triglyceride levels ≥ 150 mg/dL, or taking medications to decrease triglyceride levels, and 5) a fasting glucose level ≥ 100 mg/dL, or use of medication for treatment of hyperglycemia.

3.2.2. Biosocial factors

In terms of biosocial factors, socioeconomic status was categorized into high, middle, or low class. The educational level was categorized into less than graduation from elementary school, graduation from middle school, graduation from high school, or more than graduation from college.

3.2.3. Psychosocial factors

Emotional status and health related behaviors such as smoking, binge alcohol consumption, and physical activity was included in psychosocial factors as described in the model of Hoffman and Driscoll [11].

In terms of psychosocial factors, stress was assessed with the following question, "What is the level of daily stress?" The response was categorized into severe, a little, or not at all. Depression was assessed with the following question, "Do you currently have depression diagnosed by a psychiatrist?" Available responses were "yes" or "no." Current or past smoking habits were assessed with the following question, "Do you smoke cigarettes currently, or have you smoked cigarettes in the past?" Available responses were "yes" or "no." Binge alcohol consumption was assessed by asking Alcohol Consumption Questions which consisted of questions concerning the frequency of alcohol consumption per week [response rate: 0 (not at all)-4 points (more than 4 days in a week)], mean amount per occasion [response rate: 0 (not at all)-4 points (more than 10 glasses)], and frequency of binge alcohol consumption of more than 5 glasses of alcohol per occasion per week regardless of the type of alcohol [response rate: 0 (less than 2 glasses) -4 points (more than 10 glasses)]. The total score, with the sum of each response rate was from 0 to 12 points, and a score of more than 8 points was considered binge alcohol consumption. Physical activity was assessed using the Metabolic Equivalent Task (MET)-minutes of the International Physical Activity Questionnaire [19]. Physical activity comprising of activities performed during work and leisure periods was calculated as the sum of walking, and categorized as moderate or vigorous MET-minutes per week. Vigorous physical activity was more than 3,000 MET-minutes per week. In addition, more than 600 MET-minutes and less

than 3,000 MET-minutes per week was evaluated as moderate physical activity, and less than 600 MET-minutes per week was evaluated as light physical activity.

4. Statistical analysis

Data analysis were conducted with SPSS version 22.0 for Windows (IBM, Armonk, NY, USA). Since the KNHANES used stratified, clustered, and systematic sampling methods, sampling weight with complex samples procedures were needed to adjust for the unequal probabilities of the selection of their estimates, and to decrease the bias associated with no-response and non-coverage of the population. The characteristics of the participants, including IHD and biomedical, biosocial, and psychosocial factors, were analyzed by descriptive statistics, such as frequencies and percentages. To confirm significant biomedical, biosocial, and psychosocial factors in the development of IHD, a Rao-Scott Chi-square test was also performed. Significant biomedical, biosocial, and psychosocial factors revealed by the Chi-square test were analyzed using logistic regression. Logistic regression analysis was performed on weighted data using a complex sampling procedure to identify the factors significantly associated with the development of IHD.

Results

1. Biomedical, biosocial, and psychosocial factors of participants

The biomedical, biosocial, and psychosocial factors of participants are described in Table 1. In reference to the biomedical factors, there were 2,032 out of 3,636 women (62.7%) older than 40 years and less than 65 years. Among the participants, 2,346 women (65.8%) had a family history of hypertension, dyslipidemia, T2DM, or cerebro-cardiovascular disease. In addition, 1,360 women (39.4%) were overweight or obese, and 1,802 women (46.7%) had metabolic syndrome.

In reference to the biosocial factors, 1,729 (47.8%) women reported that their socioeconomic status was middle class. In addition, women with an educational level of less than graduation from elementary school were most common [1,702 women (41.2%)].

For psychosocial factors, more than half of the participants (2,011 women, 55.6%) experienced a little stress. In addition, 344 women (9.2%) were diagnosed with depression. Concerning current and previous smoking habits, 219 women (6.5%) were either currently smoking or had previously smoked, and 102 women (3.1%) engaged in binge alcohol consumption. Finally, women who engaged in low intensity physical activity were most common (1,818 women, 47.8%) in this study.

Table 1. Biomedical, biosocial, and psychosocial factors of participants (N = 3,636).

| Variables | | Categories | n* (%) [†] |
|--------------------------------|-----------------------|---|---------------------|
| Biomedical factors | Age (y) | 40-64 | 2,032 (62.7) |
| | | ≥ 65 | 1,604 (37.3) |
| | Family history | Yes | 2,346 (65.8) |
| | | No | 1,290 (34.2) |
| | Body mass index | Non-obesity | 2,276 (60.6) |
| | | Overweight and obese | 1,360 (39.4) |
| | Metabolic syndrome | With | 1,802 (46.7) |
| | | without | 1,834 (53.3) |
| Biosocial factors | Socio economic status | High | 813 (25.7) |
| | | Middle | 1,729 (47.8) |
| | | Low | 1,094 (26.5) |
| | Education level | Less than graduation of elementary school | 1,702 (41.2) |
| | | Graduation from middle school | 636 (18.3) |
| | | Graduation from high school | 872 (27.2) |
| | | More than graduation from college | 426 (13.3) |
| | Psychosocial factors | Stress | Severe |
| A little | | | 2,011 (55.6) |
| Not at all | | | 787 (20.4) |
| Depression | | Yes | 344 (9.2) |
| | | No | 3,292 (90.8) |
| Current or past smoking habits | | Yes | 219 (6.5) |
| | | No | 3,417 (93.5) |
| Binge alcohol consumption | | Yes | 102 (3.1) |
| | | No | 3,534 (96.9) |
| Physical activity | | Vigorous | 307 (8.9) |
| | Moderate | 1,511 (43.3) | |
| | Light | 1,818 (47.8) | |

*Unweighted; †weighted.

2. The difference in IHD development according to biomedical, biosocial, and psychosocial factors among post-menopausal women

The difference in IHD development according to biomedical, biosocial, and psychosocial factors among post-menopausal women is described in Table 2. The prevalence of biomedical factors in women over 65 years was greater among women with IHD than those without IHD ($\chi^2 = 2,949.12$, $p < 0.001$). In addition, the prevalence of women with a family history of hypertension, dyslipidemia, T2DM, or cerebro-cardiovascular

disease was greater among women with IHD than those without IHD ($\chi^2 = 12.84$, $p = 0.001$). The prevalence of overweight or obese women ($\chi^2 = 16.49$, $p < 0.001$), and women with metabolic syndrome ($\chi^2 = 44.84$, $p < 0.001$), was greater among women with IHD than those without IHD.

For biosocial factors, the prevalence of women with low socioeconomic status ($\chi^2 = 26.42$, $p < 0.001$), and an educational level of less than graduation from elementary school ($\chi^2 = 36.65$, $p < 0.001$) was greater among women with IHD than those without IHD.

Table 2. The difference in IHD development according to biomedical, biosocial, and psychosocial factors among post-menopausal women (N = 3,636).

| Variables | Categories | Ischemic heart disease | | χ^2 (p) | |
|-----------------------------------|--------------------------------|---|--------------------------------|------------------------|----------------------------|
| | | With n* (%) [†] | Without n* (%) [†] | | |
| Biomedical factors | Age (y) | 40-64 | 43 (32.5) | 1,989 (64.0) | 2949.12 (< 0.001) |
| | | ≥ 65 | 119 (67.5) | 1,485 (36.0) | |
| | Family history | Yes | 127 (79.5) | 2,219 (65.2) | 12.84 (0.001) |
| | | No | 35 (20.5) | 1,255 (34.8) | |
| | Body mass index | Non-obesity | 39 (23.5) | 1,321 (40.1) | 16.49 (< 0.001) |
| | | Overweight and obese | 123 (76.5) | 2,153 (59.9) | |
| Metabolic syndrome | With | 123 (73.6) | 1,679 (45.6) | 44.84 (< 0.001) | |
| | Without | 39 (26.4) | 1,795 (54.4) | | |
| Biosocial factors | Socio economic status | High | 22 (17.1) | 791 (26.1) | 26.42 (< 0.001) |
| | | Middle | 69 (38.2) | 1,660 (48.1) | |
| | | Low | 71 (44.7) | 1,023 (25.8) | |
| | Education level | Less than graduation from elementary school | 109 (64.8) | 1,593 (40.2) | 36.65 (< 0.001) |
| | | Graduation from middle school | 19 (14.1) | 617 (18.5) | |
| | | Graduation from high school | 21 (13.6) | 851 (27.8) | |
| More than graduation from college | | 13 (7.5) | 413 (13.5) | | |
| Psychosocial factors | Stress | Severe | 52 (34.7) | 786 (23.6) | 3,565.60 (< 0.001) |
| | | A little | 74 (45.6) | 1,937 (56.0) | |
| | | Not at all | 36 (19.7) | 751 (20.4) | |
| | Depression | Yes | 34 (22.3) | 310 (8.6) | 31.85 (< 0.001) |
| | | No | 128 (77.7) | 3,164 (91.4) | |
| | Current or past smoking habits | Yes | 16 (12.3) | 203 (6.3) | 45,548.89 (< 0.001) |
| | | No | 146 (87.7) | 3,271 (93.7) | |
| | Binge alcohol consumption | Yes | 1 (1.2) | 101 (3.2) | 1.88 (0.306) |
| | | No | 161 (98.8) | 3,373 (96.8) | |
| | Physical activity | Vigorous | 13 (9.0) | 294 (8.9) | 9.08 (0.036) |
| Moderate | | 53 (31.6) | 1,458 (43.7) | | |
| Light | | 96 (59.4) | 1,722 (47.4) | | |

*Unweighted; [†]weighted.

With respect to psychosocial factors, the prevalence of women with severe or a little stress ($\chi^2 = 3,565.60$, $p < 0.001$) and depression ($\chi^2 = 31.85$, $p < 0.001$) was greater among women with IHD than those without IHD. Finally, the prevalence of

women who were currently smoking or had previously smoked ($\chi^2 = 45,548.89$, $p < 0.001$), and who engaged in low intensity physical activity ($\chi^2 = 9.08$, $p = 0.036$) was greater among women with IHD than those without IHD.

Table 3. Associated factors with IHD among post-menopausal women (N = 3,636).

| Variable | Categories | Ischemic heart disease | | | |
|--------------------------------------|---|---|-----------|-----------|---------|
| | | aOR | 95% CI | p | |
| Biomedical factors | Age (y) (Ref. 40-64) | ≥ 65 | 2.99 | 1.87-4.80 | < 0.001 |
| | Family history (Ref. No) | Yes | 2.29 | 1.44-3.65 | 0.001 |
| | Body mass index (Ref. Non-obesity) | Overweight and obese | 1.46 | 0.91-2.32 | 0.115 |
| | Metabolic syndrome (Ref. without) | With | 1.93 | 1.27-2.95 | 0.002 |
| Biosocial factors | Socio economic status (Ref. High) | Middle | 0.86 | 0.46-1.58 | 0.929 |
| | | Low | 0.97 | 0.52-1.83 | 0.616 |
| | Education level (Ref. More than graduation from college) | Less than graduation from elementary school | 1.38 | 0.66-2.86 | 0.392 |
| | | Graduation from middle school | 1.03 | 0.45-2.39 | 0.941 |
| | Graduation from high school | 0.79 | 0.35-1.80 | 0.576 | |
| Psychosocial factors | Stress (Ref. Not at all) | Severe | 1.60 | 0.97-2.64 | 0.066 |
| | | A little | 1.05 | 0.64-1.71 | 0.860 |
| | Depression (Ref. No) | Yes | 2.56 | 1.66-3.96 | < 0.001 |
| | Current or past smoking habits (Ref. No) | Yes | 1.92 | 1.04-3.55 | 0.038 |
| Physical activity (Ref. Vigorous) | Low | 0.86 | 0.41-1.80 | 0.679 | |
| | Middle | 0.64 | 0.31-1.45 | 0.308 | |

aOR = adjusted odds ratio; CI = confidence interval; Ref. = reference.

3. Associated factors with IHD among post-menopausal women

The factors associated with IHD among post-menopausal women are described in Table 3. The following biomedical factors were all associated with IHD among post-menopausal women; aged 65 years or over, as compared to those in the age range of more than 40 years - less than 65 years [adjusted odds ratio (aOR): 2.99, 95% confidence interval (CI): 1.87-4.80, $p < 0.001$], family history of hypertension, dyslipidemia, T2DM or cerebro-cardiovascular disease (aOR: 2.29, 95% CI: 1.44-3.65, $p = 0.001$), and metabolic syndrome were all associated with IHD among post-menopausal women (aOR: 1.93, 95% CI: 1.27-2.95, $p = 0.002$). For psychosocial factors, both depression (aOR: 2.56, 95% CI: 1.66-3.96, $p < 0.001$) and smoking habits past and present (aOR: 1.92, 95% CI: 1.04-3.55, $p = 0.038$) were associated with IHD among post-menopausal women.

Discussion

This study identified the factors associated with IHD among post-menopausal Korean women at the biomedical, biosocial, and psychosocial levels. Our results revealed that the biomedical factors significantly associated with IHD of post-menopausal women were age, family history of hypertension, dyslipidemia, T2DM cerebro-cardiovascular disease, and metabolic syndrome. In a study regarding the prediction model for IHD development [8], individuals aged 40 years or more, showed an increased risk of IHD than those aged 40 years or less, and their risk of IHD rapidly increased around 60 years of age. In addition, Ahn et al [20] reported that the risk of IHD increased 2-fold among individuals aged over 65 years compared to those younger than 59 years. Men aged greater than or equal to 55 years with a family history of hypertension,

dyslipidemia, T2DM or cerebro-cardiovascular disease had a 6.9% increased risk of mortality from IHD than men without a family history of these diseases [21]. Also, according to a systematic review [22], the presence of metabolic syndrome was associated with a 2-fold increased risk and mortality of cardiovascular disease, including IHD. Similarly, in a study of Korean post-menopausal women, those with metabolic syndrome showed a 2.2-time increase in mortality from cardiovascular disease due to insulin resistance and abdominal obesity [23]. According to the International Diabetes Federation [24], adipocyte in obese abdomens produced mediating agents, such as tumor necrosis factor, leptin, adiponectin, and resistin, which induced insulin resistance. Furthermore, both abdominal obesity and insulin resistance has been significantly associated with metabolic syndrome that resulted in hypertension and lipid metabolism disturbance, which were also associated with development of IHD [24]. Likewise, post-menopausal women who have a change in fat distribution leading to fat accumulation around the abdomen, may have an increased risk of cardiovascular disease such as IHD. These factors were irrelevant to the body mass index of the women [25]. Thus, post-menopausal women over 40 years with a family history of hypertension, dyslipidemia, T2DM or cerebro-cardiovascular disease, and metabolic syndrome should be concerned about the risks of developing IHD and should have periodic screenings for the disease from healthcare providers.

Depression and a history of previously smoking were the psychosocial factors that also significantly associated with IHD in post-menopausal women. In a previous study conducted with American post-menopausal women, depression was also significantly associated with cardiovascular disease. In addition, Wassertheil-Smoller et al [13] reported that individuals with cardiovascular disease showed a 1.41-time increased risk of depression than their counterparts. Women with depression presented with a high heart rate and limited variability in heart rate, which resulted in increased morbidity of cardiovascular disease [26]. In addition, patients with depression had an increased C-reactive protein level, which was associated with damage of the coronary artery. As the C-reactive protein level was associated with a negative emotional status such as depression and anxiety [27], post-menopausal women may experience a greater incidence of severe depression due to the decreased secretion of estrogen which is involved in regulation of emotion in the brain [28]. Thus, early detection and treatment of depression may be significant in the prevention of IHD in post-menopausal women. In addition, according to a longitudinal study involving adults over 40 years old, women who previously smoked had a 2.72 times increased risk of IHD, and those currently smoking had a 2.34 times increased risk of IHD [29]. Furthermore, the negative influence of smoking on the development of IHD was more severe in women than

men [29]. Among the chemicals present in cigarettes, nicotine enhances nerve sheath materials such as catecholamine, which increases blood pressure, pulse rate, and cardiac output [30]. In addition, the intake of carbon monoxide while smoking increases the presence of carboxyhemoglobin in the body, which contributes to the development of cardiovascular disease by increasing the number of red blood cells, the viscosity of the blood, and platelet activation due to hypoxia [30]. Thus, interventions for smoking prevention and cessation would be important for the prevention of IHD.

This study contributes toward the further understanding of risk factors associated with IHD based on the biological and psychosocial backgrounds of Korean women through analysis of a large data set from the KNHANES. However, other potential associated factors were not considered during the literature review due to the limitations of the secondary data analysis and this may limit the study. Original studies involving various factors are suggested to identify factors associated with IHD among Korean post-menopausal women. In addition, this study used a cross-sectional study design which limits inferences of causality between the independent and dependent variables. Thus, a well-organized longitudinal study needs to be further investigated. Finally, a single question was used to assess the outcome variables (IHD) as well as some independent variables (e.g., stress, depression). Further studies should be conducted using objective diagnostic methods to improve the reliability and validity of the data.

Conclusion

In conclusion, older age, the presence of a family history of hypertension, dyslipidemia, T2DM or cerebro-cardiovascular disease, metabolic syndrome, a history of smoking, and depression may be risk factors of IHD in post-menopausal women. These findings suggest that healthcare providers need to be concerned about these associated factors when evaluating the risk of IHD in post-menopausal women. Furthermore, when planning intervention programs, healthcare providers should consider smoking and depression as modifiable factors that need to be managed in the prevention of IHD in post-menopausal women.

Conflicts of Interest

There were no potential conflicts of interest relevant to this article.

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