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# Diagnosis and Treatment of Depression and its Outcomes in Patients with Coronary Heart Disease (CHD): A Literature Review

## Abstract

**Background:** Studies suggested that there is an association between depression and CHD. Some studies indicated that diagnosis and treatment of depression in patients with CHD would result in a better diagnosis.

**Purpose:** The main purpose of this review is to answer this question: does diagnosis and treatment of depression result in better health outcomes in Coronary Heart Disease' (CHD) patients?

**Design:** The design of this review was based on the relationship between depression as an independent variable, and CHD as a dependent variable. Plus, the link between them was discussed in details suggesting that there is a strong evidence for association between depression and CHD.

**Diagnosis and Treatment Methods:** Different studies have used a variety of measures to diagnose depression, such as DSM-IV, PHQ-2, and PHQ-9. In addition, they have also treated depressive symptoms by using several methods, including invasive and non-invasive procedures.

**Results:** Depression was a risk factor for CHD and associated with higher mortality rates among CHD patients. Treatment of depressive symptoms in patients with CHD resulted in a better prognosis.

**Conclusion:** Treatment of depression in CHD patients has led to many positive consequences and improvements in patients' health.

**Keywords:** Coronary heart disease; Depression

Review Article

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**Ali H Alalawi* and Bart Hammig**

*University of Arkansas, Saudi Arabia*

***Corresponding author:** Ali Alalawi, University of Arkansas, Hofuf, PO Box: 486, Zip: 31982, Saudi Arabia, Tel: +966555964448; Email: aha1950@hotmail.com

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**Abbreviations:** BDI: Beck Depression Inventory; HADS: Hospital Anxiety and Depression Scale; DMS: Diagnostic and Statistical Manual of Mental Disorders; ICD: WHO International Classification of Diseases; GP: General Practitioner; MADRS: Montgomery-Asberg Depression Rating Scale; CIDI: Composite International Diagnostic Interview; SSRI: Selective Serotonin Reuptake Inhibitor; TCAs: Tricyclic Antidepressants

## Background

Over the past four decades, a lot of studies have been done on the association between depression and patients with coronary heart disease (CHD) [1]. Many studies suggested that the prevalence of depression is higher among patients with CHD compared to people without CHD [1-4]. However, a study showed that depression was not associated with developing CHD [5]. In general, the prevalence of depression is about 9.3% in patients with cardiac diseases in general [1].

A study mentioned that depression is a risk factor for CHD and it can result in complications and death [4]. Furthermore, recent studies have shown much evidence that depression is a risk factor for developing CHD, with an approximately 2-times higher risk of death [2,3]. A study mentioned that the link between CHD and depression has been well studied and he recommended that depression must be considered as an independent risk factor for developing CHD [6]. Most studies have shown that severe depressive symptoms are linked with worse cardiac diseases [1].

In addition, the global public health implications considered CHD and depression as the most common morbidities and they are often associated in an immense way [7]. Depressed people are at risk of CHD by 2-fold more than non-depressed individuals. They also have 2.5 times higher mortality rates compared to non-depressed people [8]. It was reported that patients with CHD and depression have a negative impact on psychosocial and economic activity of many countries [9].

Some researchers recommended that depression has direct and indirect negative impacts on individuals with CHD and there is a need to diagnose and treat depression in patients with CHD [1]. CHD comorbid with depression will continue as a major health condition and there is a need for an effective treatment of this health problem. Two studies mentioned that it is still unclear whether treatment of depression can lower the risk of CHD in individuals or not [10,11].

Early identification and treatment of depression in patients with CHD will enhance their wellbeing and quality of life. The American Heart Association also recommended that all patients with CHD must be screened and treated for depression frequently and this procedure will reduce the cost of their treatment [12]. Some studies reported that treatment of depressive symptoms in CHD patients reduces heart disease symptoms, morbidity, and disabilities [9].

On the other hand, other studies implied that treatment of

depression in patients with CHD did not improve cardiac outcome [13]. A study mentioned that cardiac rehabilitation centers do not consider the treatment of depression as an important factor in reducing the cardiac disease symptoms [9]. Nevertheless, treatment of depressive symptoms in cardiac patients is still under-recognized and it needs more studies and clinical practices to prove its effectiveness [14].

Based on the above findings, most studies support the presence of a strong association between depression and CHD. Some of the above studies suggested that diagnosis and treatment of depression in patients with CHD would result in reducing CHD complications and mortality rates. However, a study found that depression was not a risk factor for developing CHD [15].

The purpose of this paper is to review and discuss whether diagnosis and treatment of depression result in a better prognosis of CHD patients. I will also review and critique the previous epidemiological studies and literatures that were done in the last 6 years about this health issue and discuss their findings in detail. Finally, I will highlight some recommendations and suggest areas for future research.

## Previous studies on depression and coronary heart disease

In this review, I was focusing on adults from 18 to 60 years old. Genders, males and females, were included. Data were collected from more than 200 literatures and studies that were done on depression and CHD either directly or indirectly. The literatures, which were included in this review, have collected data from more than 570,000 people. This is considered a very convenient and large sample.

I have collected data from the previous literature reviews that were done in the last 6 years about depression and CHD. Some studies have used a random sample selection method [16], while others have another sampling method to develop a representative sample of the population [2,3]. Nevertheless, some studies have chosen to focus on either people with depression or patients with CHD [11], as a specific sample for their research [16]. A few studies have selected only people who had CHD in the past or patients with CHD for their research [17].

## Definition of depression and coronary heart disease

Depression is "a common mental disorder that presents with depressed mood, loss of interest or pleasure, feelings of guilt or low self-worth, disturbed sleep or appetite, low energy, and poor concentration" [18]. Coronary heart disease (CHD) is "a narrowing of the small blood vessels that supply blood and oxygen to the heart. CHD is also called coronary artery disease" [19].

## Sample collection

In this review, some samples were collected from different study designs that were done on both healthy people and CHD patients in different periods of time [7]. In this review, I covered 20 studies directly and approximately 543 other studies that were reviewed and discussed in the 20 studies. I collected data from Prospective (Cohort-Follow-Up) Studies, Meta-Analysis Studies, Literature Reviews, Epidemiologic Studies, Cross-Sectional Studies, Retrospective (Case-Control) Studies, and Other Studies (Table 1 and Figure 1).

**Table 1:** Study Designs Observed in This Review.

| Study Designs | Numbers | Percentage % |
|---|---|---|
| Prospective (cohort-follow-up)Studies | 228 | 40.50 |
| Meta-Analysis Studies | 179 | 31.79 |
| Literature Reviews | 47 | 8.35 |
| Epidemologics Studies | 39 | 6.93 |
| Cross-Sectional Studies | 15 | 2.66 |
| Retrospective (Case-Control) Studies | 7 | 1.24 |
| Other Studies | 48 | 8053 |
| Total | 563 | 100.00 |

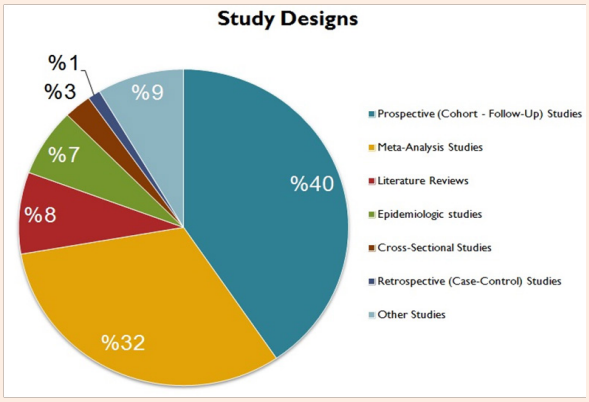


**Figure 1:** Study Designs Percentages.

A large portion of the collected samples in many studies came from administrative databases such as medical centers, health care systems, university medical centers, public health clinics [17], and global health agencies [11]. Prospective cohort studies that were done on patients with CHD were also included in this sample [7].

## Methods and Study Designs

Some cohort studies were using depression as an independent variable and CHD as a dependent variable [2,3,6,11]. However, other studies were using depression as a dependent variable and CHD as an independent variable [9,16,17]. In this review, diagnosis and treatment of depression were considered as the independent variables. CHD patients' health outcomes would be placed as the dependent variables (Figure 2).

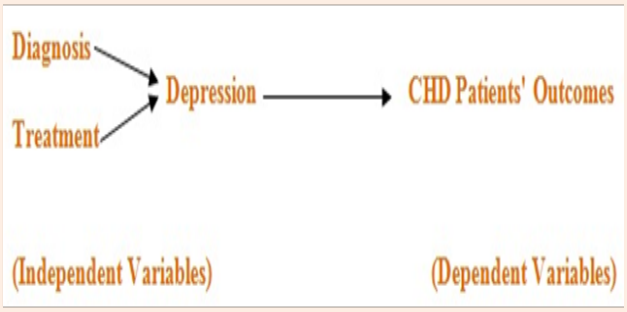


**Figure 2:** Independent and Dependent Variables.

In some studies, people were examined by clinicians to assess their health and eligibility for the study [2,3]. Other studies have used questionnaires alone with the patients' medical history [11] or with some screening instruments to diagnose depression as a risk factor [1,2,3,9]. A few other studies have measured the depression based on depressive symptoms and medications [11].

However, another study has used questionnaires with diagnostic laboratories to assess the health condition of CHD patients [16]. Furthermore, a study has applied several procedures in his study, including psychiatric interviews with the CHD patients, questionnaires, echocardiograms, and treadmill tests [17].

## The association between depression and coronary heart disease

Four meta-analyses studies have reported a high degree of evidence that depression is a risk factor for the development of CHD. Depression was also associated with high levels of morbidity and mortality among CHD patients. Some experts said that depression is common and usually coexists with CHD [4,6]. The prevalence of depression in cardiac patients is about 20%, with higher morbidity and mortality rates compared to those who do not have depressive symptoms.

In addition, a study has reviewed more than 39 prospective, meta-analyses, and epidemiologic studies that included approximately 116,000 patients who had depression and cardiac disease [4]. The results of this review supported the hypothesis that depression is considered an independent risk factor for developing CHD, with a relative risk that was 1.64 times higher compared to non-depressed individuals. The same study has also included a longer cohort study, with 19.4 years of follow-up, which showed evidence of the association between depression and high mortality rates among CHD patients.

A study mentioned that, Major depression and elevated depressive symptoms are associated with worse prognosis in patients with CHD. In fact, most studies that have examined the relationship between increasing depression severity and cardiac events have shown a dose-response relationship, with more severe depression associated with earlier and more severe cardiac events [1]. A study found that more severe symptoms of depression are linked with a higher risk of developing CHD in later years [7]. The same study has developed a new prospective about depression and CHD in their study and said that: This is the first meta-analysis to consider both etiological and prognostic studies in the depression-CHD hypothesis. In 21 etiological studies and 34 prognostic studies, totaling 146 538 participants, we found a 80% increased risk of developing CHD or dying from it (2006).

However, some of these etiological studies were biased, which resulted in reducing their power [7]. Based on a recent survey that has taken place in 60 countries with 245,404 patients with comorbid depression, depressive symptoms were strongly associated with CHD [17]. Another study that included 63,469 women concluded that the presence of depressive symptoms in healthy women was a risk factor for developing CHD in the future [11].

Cardiologists in some rehabilitation centers said that people who are depressed tend not to exercise and they were at great risk of developing cardiac events and vice versa [8]. Some researchers have studied the biological and behavioral mechanisms in order to understand the relationship between depression and CHD [2,3]. They found that depression was associated with higher cardiac morbidity and mortality rates as well.

Moreover, a study has reported that 33-64% of patients with CHD experience some depressive symptoms a few months before their cardiac disease [9]. In general, depression is very common in patients with CHD, and it has been associated with the development, progression, and mortality in CHD patients [14]. In sum, most of the above studies have proven that depression and CHD are associated and linked in many ways. Many of these studies have shown that depression is a risk factor and a predictor for the development of CHD in the future. There is also evidence that depression is related to higher morbidity and mortality rates among CHD patients. Nevertheless, a few studies suggested that the link between depressive symptoms and CHD is still not conclusive.

## Diagnosis of depression in coronary heart disease patients

There are different procedures and measures used to diagnose depression in CHD patients. The Patient Health Questionnaire (PHQ-2) and the Patient Health Questionnaire (PHQ-9) are common and frequently used diagnostic tools to diagnose depression in CHD patients [1,8,13,14,20]. Moreover, two studies suggested that depression in CHD patients can be also measured by other self-rating scales, including the Beck Depression Inventory (BDI) and the Hospital Anxiety and Depression Scale (HADS) [8,4]. Researchers sometimes use these scales with a clinician assessment to avoid possible errors.

The Diagnostic and Statistical Manual of Mental Disorders (DSM) and the WHO International Classification of Diseases (ICD) are also common diagnostic criteria used to diagnose depression. DSM and ICD are screening tools that have scales that interpret their results. In addition to DSM and ICD, some researchers have used survey and questionnaire samples for more accurate assessment of depressive symptoms in CHD patients [6].

Moreover, other studies have developed a complex model for the diagnosis of depression. They required a combination of several tests, including scaled questionnaires, diagnostic interviews, physician diagnoses, and anti-depressant medications [7]. In addition to the previous tests, another study has used more tools such as fasting blood draws, psychiatric interviews [14], echocardiograms, 24-hour ambulatory electrocardiograms, and 24-hour urine collections [17]. A few scholars have made their studies using the Center for Epidemiologic Studies Depression Scale (CES-D) [2,3,12]. They said that this instrument is useful to measure depression in community studies rather than individual studies. Additionally, two similar studies had a preference of using only three specific measures, a self-report instrument, the 9-item Patient Health Questionnaire (PHQ-9), and the Diagnostic, and Statistical Manual of Mental Disorders Fourth Edition (DSM-IV) to assess and evaluate depression in CHD patients [16,17,20].

In addition to the above measures and tools, some researchers have used the Mental Health Index (MHI-5) and the current use of antidepressant medication in order to evaluate and measure depressive symptoms [11]. Moreover, the only study that used the Hospital Anxiety and Depression Scale (HADS) and the patient's

general practitioner (GP) tests to evaluate depression in cardiac patients was done [10].

Furthermore, the Beck Depression Inventory (BDI) is a self-report inventory test for depression that has been used by some doctors [2,3]. They said that BDI is a widely used tool for the assessment of depressive symptoms in patients with CHD.

In addition, some scholars have included and discussed other diagnostic measures of depression in their review [13]. They mentioned the following tools: the self-rated Inventory of Depressive Symptoms (SR-IDS), the clinician-rated IDS (CR-IDS), Hamilton Rating Scale for Depression (HAM-D), the Montgomery-Asberg Depression Rating Scale (MADRS), the Depression Interview and Structured Hamilton (DISH), and the Composite International Diagnostic Interview (CIDI). They said that HAM-D is the most reliable diagnostic test for depression.

Differing from all the above measurement tools, another researcher has used a simple question to diagnose depression [21]. The question was "Are you depressed?" and it "has fairly high sensitivity (55%) and specificity (74%) for diagnosing depression." He also added that using a specific screening tool for the diagnosis of depressive symptoms in patients is very challenging for researchers and he preferred asking the simple question instead.

As a result of reviewing all the measures used to assess depression in CHD patients, it is clear that researchers have used a variety of tests and screening measures. The DSM-IV, PHQ-2, and PHQ-9 were frequently used and recommended more than all the other instruments. There are some controversies and arguments about the best and the most accurate diagnostic tool. I am going to talk about this issue in detail in the discussion and critique section.

## Treatment of depression in coronary heart disease patients

In this part of the review, I highlighted the different ways used to treat depression in patients with CHD, whether it is invasive (pharmacologic) or non-invasive (non-pharmacologic) treatment. I also exhibited the different types of drugs, especially antidepressants, used to cure depression and their outcomes. In general, there are many treatment options available, including antidepressant drugs, cognitive behavioral therapy, psychotherapy, and physical activity [1,8]. CHD patients can be treated by one or several means, depending on their doctors' recommendations.

## Invasive treatment (Drugs)

A researcher mentioned that Selective Serotonin Reuptake Inhibitor (SSRI) antidepressants, sertraline, paroxetine, and citalopram, are effective drugs that can reduce depression in 42% of the patients [1]. Despite that, some researchers have used SSRIs and they found no significant effect of these drugs on depressed patients [22]. Plus, they used the SSRI with a beta-adrenergic blocking agent in order to reduce the depression, but this combination increased the risk of death from CHD [11,14,17].

Two studies found that fluoxetine, sertraline, citalopram and mirtazapine are safe antidepressants that have no adverse effects on the cardiac function [8,11]. Two other studies agreed that SSRIs have the highest safety level among all antidepressants [8,14]. A researcher said that SSRIs have an advantage over TCAs and were highly recommended for treating depression, especially in patients with CHD [4]. Plus, two scholars added that fluoxetine was an effective drug in reducing depressive symptoms [11,14].

Tricyclic antidepressants (TCAs) are effective in treating depression and were recommended for cardiac patients [1,14]. However, the use of TCAs and monoamine oxidase inhibitors as a combination is contraindicated. This combination has some toxic side effects and increases the risk of death as a result. Plus, two experts mentioned that the effect of TCAs on reducing depressive symptoms is limited [22], a study mentioned that the use of TCAs should be avoided with the presence of other effective antidepressants [4]. Another study also supported these findings and they said that TCAs were not significant in reducing depression in some CHD patients [14].

Using 2 or more antidepressant drugs is not always effective for the treatment of depression. For instance, two studies agreed that using a combination of both SSRIs and TCAs was not effective in reducing depressive symptoms in CHD patients [11,22]. Ten studies have shown that omega-3 fatty acid was an effective antidepressant in treating unipolar and bipolar depressive symptoms. Similarly, some researchers used omega-3 supplements to treat depression, but they found no significant effect of omega-3 in reducing depressive symptoms in CHD patients [16].

Furthermore, a study suggested that "four or five classes of cardiac drugs have each been proven to improve survival following ACS (aspirin, beta-blockers, statins, and angiotensin-converting enzyme inhibitors/ angiotensin receptor blockers), and when all are taken regularly, mortality is reduced by about half," but this assumption was not proven to be correct and it needs to be evaluated [8].

## Non-invasive treatment (Cognitive - Exercise - Rehabilitation)

Cognitive behavioral therapy is another option for treating depression in CHD patients. It is usually used when the patient prefers not to take drugs. In fact, cognitive therapy was more efficient in treating depression than antidepressant drugs in some patients. It is highly recommended to use a combination of drugs and behavioral treatments in order to get the best results [1].

In fact, a researcher has used a combination of cognitive behavioral therapy and SSRIs in his study [8]. He also applied a combination of behavioral therapy and fluoxetine as well. The results were significantly positive in reducing depressive symptoms in CHD patients.

Physical exercise is another way to reduce the depressive symptoms in cardiac patients. It is also recommended to use a combination of exercise and another option to get better results [1]. They also said that physical treatment of cardiac patients does not give better results compared to using drugs or behavioral treatments [8].

Psychotherapy treatments were used and recommended by two studies [1,8]. In general, psychotherapy has a positive impact on depressed patients [4]. Also, another study supported these

findings and said that psychotherapy treatment has many benefits in reducing depression in patients with CHD [14]. Psychotherapy also can be used in a combination with another treatment option. But, more research and studies are needed to fulfill this area.

To sum up, depression in CHD patients can be treated by either pharmacological or non-pharmacological ways. A group of antidepressant drugs, including SSRIs are proven to be safe and effective in treating depression in CHD patients. Cognitive behavioral therapy, psychotherapy, and physical activity are also efficient in reducing depressive symptoms in CHD patients, but more studies are needed to be done on them.

Doctors' preferences and recommendations on the best treatment option were as follows: SSRIs Antidepressants, Cognitive Behavioral Therapy, Exercise and Cardiac Rehabilitation, Psychotherapy, then Other Antidepressants (Table 2 and Figure 3).

**Table 2:** Treatment Recommendations for Depression in CHD Patients.

| Treatment Option | Number of Studies Recommended | Percentage % |
|---|---|---|
| (SSRI) Antidepressants | 27 | 38.57 |
| Congnitive Behavioral Therapy | 17 | 24.29 |
| Exercise and Cardiac Rehabiliation | 12 | 17.14 |
| Psycotherapy | 8 | 11.43 |
| Other Antidepressants | 6 | 8.57 |
| Total | 70 | 100.00 |

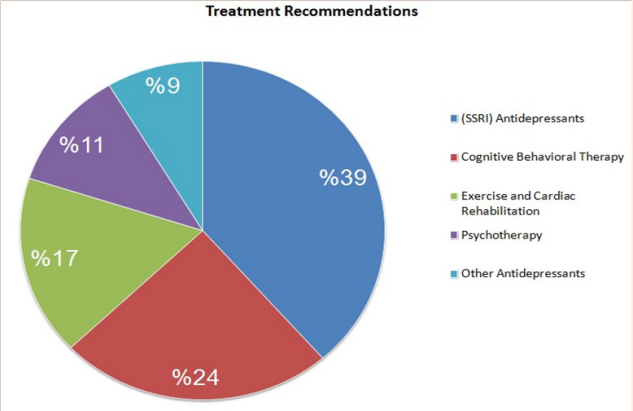


**Figure 3:** Treatment Recommendations Percentages.

## Results and Findings

Diagnosis and treatment of depression is essential in CHD patients in improving their overall health and wellbeing. However, the health setting practices might affect its efficiency either positively or negatively [12]. A scholar said that diagnosis and treatment of depression in patients with CHD are important for a better prognosis [4]. A study supported these findings and said that accurate diagnosis and proper treatment of depression is important in CHD patients [14].

CHD patients must be screened for depression frequently. If they show positive results for depressive symptoms, they should be treated. Also, doctors and clinicians should monitor the progress of the treatment course to avoid the undesirable outcomes [1]. Another study added that early detection of depression is important for a better management and prognosis of patients with CHD [9].

Moreover, a review suggested that screening of depression in CHD patients resulted in better outcomes [8]. People who showed positive results tended to seek treatment for their depression. As a result, they had a lower risk of cardiac events and better prognoses as well. Physical therapy was proven to reduce depression in CHD patients. In general, increased physical activity resulted in better outcomes in these patients [17].

Unlike the above findings, a study mentioned that "although evidence is strong that treatment with medication or cognitive therapies improves symptoms of depression, evidence is lacking for a significant effect of such interventions on cardiac outcomes." Plus, CHD patients with depression must be screened in early stages for better management and interventions [21].

Altogether, based on the above findings, most studies suggested that treatment of depression in CHD patients had many positive consequences. They also supported the use of both antidepressant drugs and behavioral therapy as effective methods for treating depressive symptoms. Most studies also reported that treatment of depressive symptoms was associated with lower mortality rates in cardiac patients. A few studies suggested that more research is needed for a better understanding of the link between treating depression and cardiac outcomes.

## Discussion

Some researchers have done a review of more than 100 studies about depression and CHD patients [4]. They came up with the evidence that diagnosing and treating depression has significantly improved the outcomes of CHD patients. They also mentioned that treatment of depressive symptoms was important not only in CHD patients, but also in all heart disease patients.

Another review based on the American Heart Association Science Advisory, included that diagnosis and treatment of depressive symptoms was associated with improvement in CHD patients' health [1]. This review covered more than 60 prospective studies about depression and cardiac diseases, which makes it powerful and reliable.

Nevertheless, the findings of this review are correct with most, not all, cardiac patients. For instance, some depressed patients showed no response to the antidepressant treatment [1]. They represent a small percentage, but researchers should consider them and try to find other possible treatments. In addition, a study [8] supported the findings of two other studies [1,4], saying that screening and treating of depression had reduced the risk of CHD mortality and improved the prognosis in cardiac patients. This study also emphasized the role of screening to detect depressed CHD patients [8]. They also said that some patients had a mild form of depression, and they would be detected only by screening.

Two additional studies supported the above findings, suggesting that routine screening must take place in all health care settings that deal with CHD patients specifically [9,12].

Another review has observed lots of studies related to treatment of patients with CHD [14]. It suggested that all different treatment methods were effective to treat depressive symptoms in CHD patients. The treatment means were recommended, including pharmacologic treatments, psychotherapeutic interventions, exercise programs, and behavioral therapies.

More and more, a study mentioned that "several large-scale studies have clearly documented that increased physical activity reduces cardiovascular events, but whether exercise interventions can eliminate the excess risk of cardiovascular events associated with depressive symptoms has not been studied." But this hypothesis does not seem to be steady for many reasons. First, this study talked about cardiovascular diseases in general, not concerning CHD specifically. Second, many other studies have supported the fact that physical activities were associated with better health outcomes in CHD patients. Finally, a study also said that their "findings raise the possibility that increased exercise may decrease the risk of cardiovascular events associated with depression [17]."

Additionally, a study mentioned that antidepressant treatment might lead to worse depressive symptoms and it has no significant change on the mortality rates among CHD patients [20]. However, this study has some limitations. First, participants were not diagnosed for the presence of other health conditions such as diabetes, hypertension, or anxiety, and the results might be confounded. Plus, this study focused only on Caucasian females and it could be biased. Because of these limitations, we cannot rely on the findings of this study.

A review mentioned that "treatment of depression in patients with CHD does not improve cardiac outcome. We hypothesize that the weaknesses of depression assessment and treatment strategies in subjects with comorbid CHD is an important contributing factor to this apparent paradox." They concluded that "lack of uniformity in methods and scales used to assess depression across studies makes it impossible to consolidate findings [13]", which supported their hypothesis that the error was not related to the treatment but the assessment of depression. They also proposed that there should be one method to assess depression in CHD patients and it should be generalized to all health care sittings.

## Summary and Conclusion

As a result of this review, depression was a risk factor for coronary heart disease (CHD) and associated with higher mortality rates among CHD patients. Many measures were used to diagnose depression in CHD patients, but the most reliable and frequently used tools were the PHQ-2, PHQ-9, and DSM. There are many options for treating depression, including antidepressant drugs, cognitive behavioral therapy, psychotherapy, and physical activity. These options are all effective and the most recommended pharmacologic drugs were the SSRIs group.

Most of the observed literature suggested that diagnosis and treatment of depressive symptoms in CHD patients resulted in better health outcomes and lower mortality rates. Few studies mentioned that the treatment of depression did not improve the CHD patients' prognosis. But, these studies were confounded, biased, and had some limitations.

## Recommendation and Looking to the Future

First, health care providers should have a routine screening procedure to diagnose depression in all CHD patients [1,4]. Second, monitoring CHD patients during the treatment course is important to avoid both adverse drug reaction and for drug efficacy [1]. Third, routine practices, that deal with CHD patients, were poor in most health care settings and need to be improved with new interventions, including professional supervision, monitoring, and management [8,10]. Further research on the antidepressant drugs and their effectiveness is needed in order to develop the best treatment options for CHD patients. Further studies of the health care interventions and collaborative programs are important to improve health outcomes in CHD patients [14].

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